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American Therapeutic Society

Organized, May 1, 1900
Incorporated, July 7, 1904

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Name	Specialty	Title	Societies	Address
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8. Bainbridge, William Seaman	Surgeon	Prof. Surg., N. Y. Polyclin. Sch. & Hosp., Surg. Skin and Cancer Hosp., etc.	Am. Asso. Obstet. & Gyn., A.M.A.	34 Gramercy Park, New York, N. Y.
9. Barbat, John Henry	Surgery	Instruct. in Surg. Anat. Univ. of Cal., etc.	A.M.A.	275 Post St., San Francisco.
10. Barnes, Noble P.	Materia Medica	Prof. Mat. Med. & Ther., Geo. Wash. Univ., Washington, D. C., Chief of Service, Casualty Hosp., etc.	F.A.C.P., A.M.A.	The Arlington, Washington, D. C.
11. Beates, Henry, Jr.	State Medicine	Ex-Pres. Nat. Confed. of State Examining Boards, etc. Ex-Pres. State Bd. Med. Exam.	A.M.A., Amer. Acad. of Polit. Sciences., Am. Acad. Med.	260 S. 16th St., Philadelphia, Pa.
12. Bishop, Louis Faugeres	Diseases of Chest	Prof. Dis. of Heart, etc., Fordham Univ., Phys. to Lincoln Hosp., etc.	A.M.A. F.A.C.P.	109 E. 61st St., New York, N. Y.

13. Blackader, Alexander Dougall	Pharmacol & Ther., & Dis. of Children	Lect. Dis. of Child. & Prof. Ther. & Pharm., McGill Univ., Phys. to Children's & Montreal Gen. Hosps., etc. Pres. Can. Med. Asso.	A.M.A., Amer. Phys., Amer. Climat.	236 Mountain St., Montreal, Canada.
14. Bleh, N. L.	Surgery	Prof. Clin. Surg. Univ. Med. School, Oklahoma City.	F.A.C.S., A.M.A.	606 State Bank Bldg. Oklahoma City, Oaklahoma.
15. Bonney, Sherman Grant	Internal Medicine	Prof. Med., Univ. of Colorado, Visiting Phys. to St. Luke's Hosp., etc.	A.M.A., Amer. Climat.	Stedman Bldg., Denver, Col.
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19. Camp, Carl Dudley	Neurology	Prof. Nervous Diseases, Univ. of Michigan, etc.	A.M.A., Neurol. Asso., Asso. Path & Bact.	304 So. State, Ann Arbor, Mich.
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22. Cheney, William J.	Internal Medicine	Clin. Prof. Medicine, Leland Stanford, Jr. Univ., etc.	A.M.A.	Shreve Bldg., San Francisco, Cal.
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25. Da Costa, John C., Jr.	Internal Medicine	Assoc. Prof. Medicine Jefferson Med. Coll., Phys. to Jefferson Hosp., etc.	A.M.A., Amer. Phys.	1529 Pine St., Philadelphia, Pa.
26. Davies, Bertram C.	Ear, Nose & Throat	Instructor in Dis. of Ear, Nose & Throat, P. & S. Med. Coll., Los Angeles, Cal.	A.M.A.	Title Insurance Bldg. Los Angeles, Cal.

27. Dawes, Spencer Lyman	Mat. Med. & Therapeutics	Formerly Adj. Prof. Mat. Med. & Ther., Albany Med. Coll., Director of Laboratory, Albany Coll. of Pharmacy.	A.M.A.	Room 703, Hall of Records, New York, N. Y.
28. Davis, Nathan S.	Medicine	Prof. Medicine North-West. Univ. Med. Sch., Phys. to Mercy and other hospitals.	A.M.A.	7 West Madison St., Chicago, Ill.
29. Duke, William W.	Experimental Medicine	Prof. Experimental Medicine. Univ. of Kansas, etc.	A.M.A.	406 Waldheim Bldg., Kansas City, Mo.
30. Evans, George Herbert	Medicine	Assist. Prof. Clinical Medicine, Univ. of California, etc.	A.M.A.	133 Geary St., San Francisco, Cal.
31. Fick, Edward P.	Internal Medicine	State Bacteriologist of Washington.	A.M.A.	718 Cobb Bldg., Seattle, Wash.
32. Fisher, Edward D.	Neurology	Prof. Mental & Nervous Dis., N. Y. Univ. Med. Sch., Neurologist & Alienist, Bellevue Hosp.	A.M.A., Amer. Neu. Asso.	46 East 52nd St., New York, N. Y.
33. Freeman, Elmer B.	Medicine	Asst. Prof. Clinical Medicine, Univ. of Maryland, etc.	A.M.A.	412 Cathedral St., Baltimore, Md.
34. Freund, Hugo A.	Medicine	Asst. Prof. Medicine, Detroit Med. Coll., Attg. Phys. to Harper Hosp., etc.	A.M.A., Asso. Path. & Bact.	355 Woodward Ave., Detroit, Mich.
35. Friedenwald, Julius	Gastro-Enterology	Prof. Gastro-Enterology, Univ. of Maryland, Phys. to Mercy Hosp., etc.	A.M.A., Amer. Phys.	1013 N. Charles St., Baltimore, Md.
36. Gompertz, Louis M.	Internal Medicine	Clin. Instructor in Gastro-Intest. Dis., Attg. Phys. Univ. Clin.	A.M.A.	1195 Chapel St., New Haven, Conn.
37. Gordinier, Hermon, C.	Internal Medicine	Prof. Medicine, Albany Med. Sch., Union Univ., Phys. to Samaritan Hosp., etc.	A.M.A., Amer. Phys. Amer. Neurol.	89 Fourth St., Troy, N. Y.
38. Gordon, Andrew R.	Internal Medicine	Assoc. Prof. Clinical Medicine, Univ. of Toronto.		345 Bloor St., West Toronto, Canada.
39. Greene, Charles Lyman	Internal Medicine	Formerly Prof. Medicine, Univ. of Minn., Phys. St. Luke's Hosp., etc.	F.A.C.P., A.M.A., Amer. Phys.	150 Lowry Arcade, St. Paul, Minn.
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42. Hare, Hobart Amory	Therapeutics and Diagnosis	Prof. Therapeutics and Diagnosis, Jefferson Med. Coll., etc.	A.M.A., Amer. Phys.	1801 Spruce St., Philadelphia, Pa.

43. Heard, James Delavan	Internal Medicine	Prof. Medicine, Univ. of Pittsburgh, etc.	A.M.A.	6101 Penn Ave., Pittsburgh, Pa.
44. Hemmeter, John C.	Physiology and Medicine	Prof. Physiology & Clin. Medicine, Univ. of Maryland; Director Physiological Laboratory.	A.M.A., Amer. Gastro-Ent. Soc. A.A.A.S., F.R.S.A., (England)	739 University Pkway, Baltimore, Md.
45. Hertzler, Arthur E.	Surgery	Prof. Surgery, Med. Coll. Univ. of Kansas; President Halstead Hosp.	A.M.A., Soc. Amer. Anat.	Rialto Bldg., Kansas City, Mo.
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47. Hoxie, George H.	Internal Medicine	Attg. Phys. German Hosp. & Tuberc. Ward, K. C. Gen. Hosp.	A.M.A., Amer. Acad. of Med.	624 Rialto Bldg., Kansas City, or Kansas City Base Hosp. No. 28.
48. Hutcheson, J. Morrison	Internal Medicine	Prof. Int. Med., Med. Coll. of Va., Phys. to Memorial Hosp, and Johnson and Willis Sanitorium.	A.M.A., A.S.I.S.	608 Professional Bldg., 5th & Franklin Sts., Richmond, Va.
49. Jennings, Charles Godwin	Internal Medicine	Prof. Medicine, Detroit Med. Coll., Phys. to Harper Hosp., Pres. Detroit Clin. Laboratory.	A.M.A., Amer. Ped. Soc., Amer. Clim. Asso.	435 Jefferson Ave., Detroit, Mich.
50. Johnson, Frank Seward	Internal Medicine	Prof. Medicine, North-West. Univ., Consult. Phys. to Michael Reese Hosp., etc.	A.M.A., Amer. Clim. Asso.	2521 Prairie Ave., Chicago, Ill.
51. Juettner, Otto	Therapeutics	Prof. Clin. Medicine, Cincinnati Polyclinic & Post-Grad. Med. Sch., etc.	A.M.A, Amer. Acad. of Med.	2164 Elysian Pl., Cincinnati, Ohio.
52. Katsuki, Ichitaro	Internal Medicine		A.M.A.	176 N. Vineyard St. Honolulu, Hawaii
53. Kemp, Robert Coleman	Gastro-Enterology	Formerly Prof. Gastro-Ent. Dis., New York Sch. of Clin. Med., Consulting Phys. Gastro-Ent. Dis., Manhattan State Hosp., etc.	A.M.A.	103 East 57th St., New York, N. Y.
54. Kirk, William Jr.	Internal Medicine	Instructor in Med., Albany Med. School, Union Univ.		2167 Fifth Ave., Troy, N. Y.
55. Leech, D. Olin	Internal Medicine, Obstet., Surg.	Obstetrician Florence Crittenden Home, Chief of Staff Internal Medicine, Eastern Dispensary & Casualty Hosp., etc.	A.M.A.	1237 Massachusetts Ave., Washington, D. C.
56. MacFarlane, Andrew	Internal Medicine	Clinical Prof. Medicine Med. Sch. of Union Univ., Assist. Attg. Phys. Albany Hosp.	A.M.A.	198 Washington Ave. Albany, N. Y.

57. McGuire, Stuart	Surgery	Prof. Surg. & Dean Med. Coll. of Va., Surg. in charge St. Lukes', and Vis. Surg. Memorial Hosp.	Sou. Surg. & Gyn. Soc. Tri-State Med. Soc., A.M.A.	513 E. Grace St., Richmond, Va.
58. McGuire, Edward	Internal Medicine	Prof. Internal Med., Med. Coll. of Va.		6 E. Franklin St., Richmond, Va.
59. Mattison, F. C. E.	Surgery	Prof. Surgery, Univ. of South. California, Surg. to Los Angeles Co. Hosp.	A.M.A., Amer. Coll. of Surg.	Chamber of Commerce Bldg., Pasadena, Cal.
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62. Mills, R. Walter	Internal Medicine	Assoc. in Medicine, Washington Univ., St. Louis.	A.M.A., Am. Gastro-Enter. Ass'n.	6682 Oakland Ave., St. Louis, Mo.
63. Milroy, William Forsythe	Internal Medicine	Prof. Clin. Medicine, Univ. of Nebraska, Visit. Phys. Clarkson Memorial Hosp.	A.M.A.	The Colonial, Omaha, Neb.
64. Morgan, Francis P.	Internal Medicine			The Toronto, Washington, D. C.
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70. Pottenger, Francis Marion	Internal Medicine	Prof. Diseases of Chest, Univ. of South. Cal., Director Pottenger Sanatorium.	A.M.A.	Title Ins. Bldg., Los Angeles, Cal.
71. Reilly, Thomas Francis	Internal Medicine	Prof. Theory & Pract. Fordham Univ., Asst. Attg. Phys. Bellevue & Allied Hosp., etc.	A.M.A., F.A.C.P.	220 West 139th St., New York, N. Y.

72. Richardson, James Julius	Ear, Nose & Throat	Prof. Otology, Laryng. & Rhinol., Howard Univ. Sch. of Med., Washington, D. C.	A.M.A.	1509 Sixteenth St., Washington, D. C.
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74. Rottenberg, I. Morvay	Internal Medicine	Phys. to St. Mark's Hosp., etc.	F.A.C.P.	105 West 118th St., New York, N. Y.
75. Roussel, Albert, E.	Internal Medicine	Associate Prof. of Med., Medico-Chir. Grad. School, U. of P., and Vis. Phys. Med.-Chir. and Howard Hosps.	A.M.A., F.A.C.P.	2108 Pine St., Philadelphia, Pa.
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79. Satterthwaite, Thomas Edward	Internal Medicine	Formerly Prof. Medicine N. Y. Post-Grad. Med. Sch. & Hosp., Consulting Phys. Post-Grad. and other hospitals.	F.A.C.P., A.M.A.	7 East 80th St., New York, N. Y.
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84. Stewart, Francis E.	Materia Medica	Prof. Mat. Med., Medico-Chir. Univ.	A.M.A.	11 West Philellena Phila., Pa.
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88. Thornton, Edward Quin	Materia Medica	Assist. Prof. Materia Jefferson Med. Coll., Phys. to the Hosp.	A.M.A.	1331 Pine St., Philadelphia, Pa.
89. Timme, Walter	Neurology	Asst. Phys. Neurol. Institute.	Am. Neurol., N. Y. Acad. of Med., A.M.A.	153 W. 72nd St., New York, N. Y.
90. Vander Veer, Albert,	Surgery	Emeritus Prof. Surg. Albany Med. Coll., Amer. Surg.-in-chief Albany Hosp., etc., Ex-Pres. A. M. A.	A.M.A., Amer. Surg. Ass'n.	28 Eagle St., Albany, N. Y.
91. Van Rens-salaer, Howard	Internal Medicine	Formerly Prof. Med. Albany Med. Coll., Tuberculosis Expert U. S. A.	A.M.A.	5 Spruce St., Albany, N. Y., or Camp Johnson, Jacksonville, Fla.
92. Wheatley, Frank George	Therapeutics	Prof. Mat. Med. & Ther., Tufts Coll., Boston Mass.	A.M.A.	174 N. Adams St., North Abington, Mass.
93. White, John Blake	Surgery	Surg. Co. Prison N. Y. City; Consult. Surg. Littleton Hosp., New Hampshire.	A.M.A.	1013 Madison Ave., New York, N. Y.
94. Wilcox, Reynold Webb	Internal Medicine	Formerly Prof. Med. N. Y. Post-Grad. Med. Sch. & Hosp., Consult. Phys. to St. Mark's and other Hospitals.	Am. Cong. on Internal Med., F.A.C.P., Am. Asso. Med. Jour.	679 Madison Ave., New York, N. Y.
95. Wiley, Harvey W.	Chemistry	Prof. Agricultural Chem., Geo. Wash. Univ.	Amer. Chem. Soc.	Cosmos Club, Washington, D. C.
96. Wilson, James Cornelius	Internal Medicine	Emeritus Prof. Medicine Jefferson Med. Coll., Phys.-in-chief Lankenau Phys. Hosp., Consult. Phys. various hospitals.	A.M.A., Amer. Phys.	1509 Walnut St., Philadelphia, Pa.
97. Wood, Horatio C., Jr.	Internal Medicine	Prof. Pharmacology & Therap. U. of P., Vice Chairman Revision Co. of U. S. P.	A.M.A., Amer. Phar. Ass'n.	434 South 44th St., Philadelphia, Pa.
98. Zueblin, Ernest	Internal Medicine	Assoc. Prof. of Medicine, Univ. of Cincinnati. Med. Director Cinn. Tuberc. Sanatorium.	A.M.A., F.A.C.P.	Cincinnati Tuberculosis Sanatorium, Pine Hill, Cinn., O.
99. Tucker, Beverley R.	Neurology & Psychiatry	Prof. Neurology & Psychiatry Med. Coll. of Virgina.		212 W. Franklin St., Richmond, Va.

100. Vander Hoof, Douglas	Internal Medicine	Prof. of Practice, Med. Coll. of Virgina.	F.A.C.P.	

To Fill Vacancies

1. McCrudden, Francis H.	Biology, Chemistry, & Internal Med.	Asst. Prof. of Applied Therapeutics.		Robert B. Brigham Hosp., Boston, Mass.
2. Diner, Jacob	Diagnosis & Therapeutics	Prof. Clin. Diagnosis, Pharmacol. etc., Consulting Phys. to various hospitals.		316 W. 84th St., New York, N. Y.
3. Mercur, William H.	Internal Medicine	Phys. to several hospitals.	F.A.C.S.. A.M.A., A.A.I.S., Am. Clim.	5244 Fifth Ave., Pittsburgh, Pa.

In Foreign Service

1. Kiliani, Otto, G. T.	Surgery	Prof. Clinical Surgery, Columbia Univ. Surg. German Hosp., etc.	Amer. Surg. Ass'n.	44 West 77th St., New York, N. Y.
2. Rudolf, Robert Dawson	Therapeutics	Prof. of Therapeutics, Phys. General Hosp., Toronto.		302 Bloor St. W., Toronto, Canada.

EX-PRESIDENTS

Horatio C. Wood	Philadelphia, Pa.	1900-1	Harvey W. Wiley	Washington, D. C.	1910-11
Reynold Webb Wilcox	New York, N. Y.	1901-2	Alexander D. Blackader	Montreal, Can.	1911-12
Thomas E. Satterthwaite	New York, N. Y.	1902-3	Noble P. Barnes	Washington, D. C.	1912-13
*Howard H. Barker	Washington, D. C.	1903-4	Howard van Rensselaer	Albany, N. Y.	1913-14
Oliver T. Osborne	New Haven, Conn.	1904-5	Francis M. Pottenger	Los Angeles, Cal.	1914-15
*Carl Beck	New York, N. Y.	1905-6	Robert T. Morris	New York, N. Y.	1915-16
*Robert Reyburn	Washington, D. C.	1906-7	Josiah N. Hall	Denver, Colo.	1917-18
*John V. Shoemaker	Philadelphia, Pa.	1907-8			
Frederic H. Gerrish	Portland, Me.	1908-9			
James C. Wilson	Philadelphia, Pa.	1909-10			

*Deceased.

DECEASED MEMBERS

Samuel Claggett Busey, M.D., LL.D., died Oct. 19, 1899.
William P. Manning, M.D., died Feb. 9, 1901.
John Thomas Winter, M.D., LL.D., died June 22, 1902.
George Edward Tyler, M.D., died July 7, 1902.
Robert Henderson Graham, M.D., died Aug. 24, 1903.
George Bingham Fowler, M.D., died March 6, 1907.
John S. McLain, M.D., died June 2, 1907.
Robert Reyburn, M.D., died March 25, 1909.
Justin Steer, M.D., died March 25, 1909.
Howard H. Barker, M.D., died May 8, 1910.
John Veitch Shoemaker, M.D., died October 11, 1910.
Carl Beck, M.D., died June 8, 1911.
Henry Alered Robbins, M.D., died October 26, 1911.
John Herr Musser, M.D., died April 3, 1912.
Louis Nelson, A.M., M.D., died April 14, 1912.
Frederick Forchheimer, M.D., died June 1, 1913.
Louis Kolipinski, M.D., died December 14, 1914.
Charles E. Woodruff, A.M., M.D., died June 13, 1915.
Peter Brynberg Porter, A.M., M.D., died August 5, 1915.
Henry L. Elsner, M.D., died February 17, 1916.
Julius H. Eichberg, M.D., died November 2, 1916.
George Ben Johnston, M.D., died December 20, 1916.
Heinrich Stern, M.D., died January 30, 1918.
Jacob Friedman, M.D., died April 13, 1918.

EIGHTEENTH ANNUAL MEETING

Held at the New York Academy of Medicine,
New York City

June 1 and 2, 1917.

Dr. J. N. Hall, of Denver, Colo., in the Chair.

REPORT OF COMMITTEE ON ADMISSIONS

DR. THOMAS E. SATTERTHWAITE, Chairman.

ADDRESS OF WELCOME

The Address of Welcome was delivered by Dr. Reynold Webb Wilcox. In one of his happiest veins he extended the hand of brotherly love and hospitable welcome to all the members and expressed the regret that the Mayor of New York was not close enough to either the people or to science to perform this duty. Dr. Wilcox pointed out the importance of Therapeutics both to the patient and to the Medical Profession and emphasized the fact that the neglect of this branch of Medicine is responsible to no small extent for the many cults and drugless healers which have come into prominence. The value of the work done by this Society and its members was emphasized by the speaker who dwelt also in most eloquent terms on the duty of the physician towards the public. The well chosen words and the deep thoughts expressed by the speaker were received enthusiastically by all members present.

RESPONSE TO THE ADDRESS OF WELCOME

DR. O. T. OSBORNE,

NEW HAVEN, CONN.

We all appreciate the overwhelming good fellowship of Dr. Wilcox: we are all glad we came and we are glad to remain. The Society always loves to come to New York—New York is the Mecca.

OBITUARIES

GEORGE BEN JOHNSTON, M.D., LL.D.

BY J. MORRISON HUTCHESON, M.D.,

RICHMOND, VA.

George Ben Johnston was born July 25, 1853, in the town of Tazewell in the section known as Southwest Virginia, where his boyhood and a part of his early manhood were spent. He came of sturdy pioneer stock and numbered among his forbears soldiers, statesmen and physicians of note. His academic training was obtained at the University of Virginia, where he also studied medicine for one year, completing his course at the University of the City of New York with the class of 1876. After two years of practice in the town of Abingdon, Virginia, he removed to Richmond where he resided until his death December 20, 1916.

Dr. Johnston was twice married, in 1881 to Miss Mary McClung, who died the following year, and in 1892 to Miss Helen Rutherford who with four children survives him. He was a singularly devoted husband and father, and his home, his great source of pride and joy, will be long remembered by hundreds whose fortune it was to share its hospitality.

Early in life Dr. Johnston evinced that liking and talent for surgery which determined his professional career. Always an ingenious and skilful operator, and possessed of unusual clinical instinct linked with the courage of the pioneer, as the years went by he attained an accuracy and precision of judgment which to his younger colleagues seemed little short of marvelous. In 1879, he performed the first operation done under Listerism in the State of Virginia, and with discerning eye he was ever on the alert and ready to adopt those innovations which appealed to him as sound. In 1884 he was elected Professor of Anatomy in the Medical College of Virginia, and in 1893 Professor of Surgery. When in 1913 the Medical College of Virginia and the University College of Medicine were amalgamated, he became head of the department of Surgery in the new institution, a position which he resigned two years before his death to become a member of the Board of Visitors, where he served as one of the Executive Committee. His services to medical education in Virginia and the South can never be measured. For years he was the central figure in every movement for progress and the guiding spirit in the institution with which he was connected.

Though surrounded by arduous and exacting duties, Dr. Johnston found time to produce a number of noteworthy contributions to surgical

literature. His style was attractive, his ideas forcefully presented, and though he was by no means a prolific writer, his works occupy a conspicuous and lasting place in the records of surgical progress.

Dr. Johnston was an honored member of this Society, holding at the time of his death the office of vice president. He was, at various times, president of the American Surgical Association, president of the Southern Surgical and Gynecological Association, president of the Norfolk and Western Railway Surgeons Association, president of the Richmond Academy of Medicine and Surgery, president of the Medical Society of Virginia, member of the House of Delegates and of the Judicial Council of the American Medical Association, delegate from the American Surgical Association to the International Medical Congress at Madrid in 1913 and delegate from the United States to the International Periodical Gynecological Congress in 1896. A list of the positions he filled is thus, in a sense, a chronicle of the professional advance of his life time.

While the foregoing details denote a life of vigor and usefulness far beyond the ordinary, they fail to indicate those distinctive qualities of personality so difficult to portray. In Dr. Johnston there was combined a dominant strength, which friends leaned on and foes respected, with a gentleness of spirit which encouraged the appeal of the weakest. His courtly and gracious manner, his distinguished appearance and elegance of poise were such that men instinctively paid him deference, yet he was entirely at home in any company and his friends represented every class from the highest to the lowest. He was a charming conversationalist, always an attentive and interested listener, while his ability to relate an appropriate anecdote was unsurpassed.

When George Ben Johnston breathed his last, one of the master spirits of his generation passed from the earth. Few have been endowed by nature with more brilliant or diversified talents, and few indeed have attained the degree of personal power that was his; yet it may be truly said of him that "In all the glorious gifts that God Almighty gave him, not one was ever bent in willing service to unworthy cause."

JULIUS H. EICHBERG

BY CHARLES D. AARON, Sc.D., M.D.,

DETROIT, MICHIGAN.

Julius H. Eichberg was born in Petersburg, Va., in 1859, and died in Cincinnati, Ohio, November 1, 1916. In his early youth he studied in Germany, completing the course in the gymnasium. Thus was laid the foundation of the scientific attainments and exemplary scholarship which distinguished his later years.

In 1880 he was graduated from the Cincinnati College of Pharmacy, after having been associated in chemical laboratory work with the elder Fennel, a noted pharmacist in those days. Eichberg must have been a student of rare assiduity and talent, for he carried off honors and a gold medal at his graduation. In 1887, in recognition of his ability, he was appointed pharmacist of the City Hospital. He was not satisfied, however, with his educational equipment, despite public recognition and encouragement. In 1891 he registered as a student in the Miami Medical College; four years later he became an interne at the City Hospital, and after a short service in that capacity went to Vienna to pursue special studies. Upon his return he engaged at once in the practice of his new and what was destined to be his life-long profession, and soon won the confidence of his patients and the respect of his colleagues.

It was natural for him that he should continue his helpful work as pharmacist in the capacity of Professor of Pharmacology in the College of Pharmacy, but he soon added to his academic labors those of Professor of Materia Medica and Therapeutics in the Ohio Miami College, now the University of Cincinnati. In the Cincinnati Hospital he took an unusually active part in the contagious diseases department. His students speak of him as one who "won a lasting place in their hearts," and the Medical and Surgical Staff of the Bethesda Hospital, of which he was a member, declare "His high medical attainments have always been recognized." They also pay a tribute to his "courteous, genial and modest personality." The faculty of the University of Cincinnati College of Medicine records that "he was one of its most loyal, farseeing, and honest members," and that "he was a man of rare scientific attainments and most modest demeanor"; and it asserts, what every one who was in professional touch with him will endorse, that "he possessed an intimate knowledge of pharmacy, chemistry, and medicine," such as made his death "an almost irreparable loss." While his associates respected him for his scrupulous and strictly scientific judgment, his patients esteemed him because of his transparent honesty and unswerving loyalty. He had rare acumen and diagnostic and therapeutic

ability of a high order, and these he placed at the service not only of his patients but of his colleagues with a splendid liberality.

As a man and a friend he is gratefully remembered. His tender and sympathetic nature sweetened his manly character and held those who knew him best in genuine fellowship. He possessed an analytic mind which faced the problems of social and public life with the same penetration as that by which he solved the problems of his chosen science, and he devoted himself to every allotted task with the unflagging energy with which he carved his career to professional eminence and public affection.

In addition to being a thoroughly scientific man and an excellent physician, he was also a humanitarian. The needy had a good friend in him, and the memory of his personal influence and help lingers on in many hearts and lives. His was a life of many-sided usefulness, and the Cincinnati community will long cherish it as one of signal merit.

SCIENTIFIC PROCEEDINGS*

VICE-PRESIDENT, DR. EDWARD D. FISCHER, in the Chair.

ADDRESS OF THE PRESIDENT

A Consideration of the Merits of Medical and of Surgical Treatment Respectively in Peptic Ulcer

DR. J. N. HALL,

DENVER, COL.

Unfortunately, physicians, like other men, too frequently tend to see one side of the shield only, and this tendency is perhaps as conspicuous in the decision regarding the method of treatment of peptic ulcer as in any other medical problem.

I should say at once that in my opinion there are definite and positive advantages and disadvantages pertaining to medical and to surgical treatment in various cases, and the course to be followed in any given case should be decided upon only after careful consideration of these factors.

Let us consider first the various types of ulcer, as viewed from a therapeutic standpoint, especially as to the possibility of cure by either mode of treatment. Nearly all clinicians would agree that an acute ulcer with little infiltration about its base may be expected to heal if it can be placed at relative rest, and freed from the corrosive action of an oftentimes overstrong gastric juice, and so maintained for a period of several weeks. Freedom from serious cicatricial contraction and from notable adhesions may be expected in such cases, so that, practically speaking, a complete restitution is attainable.

At the opposite extreme we may place the chronic ulcers with thickened base, oftentimes with extensive adhesions, and in the more serious cases with such chronic perforative processes as involve even excavation into the liver, or penetration of a portion of this organ or of the

*It is to be understood that the Society does not hold itself responsible for any views expressed by the readers of papers or participants in discussions.

pancreas for example, into the cavity of the stomach through the large perforative opening, with, naturally, the most extensive and firm adhesions roundabout. Only a hopeless optimist could look for favorable results in these cases from medical treatment, for even with the best of surgery the outlook is none too favorable.

Between these two types we may place the majority of ulcers coming under the observation of the internist. The milder ones, with history of a short course in many cases, with no notable thickening, adhesions, or deformity of the canal (when these features can fortunately be determined), are certainly "medical ulcers" at the start, and many of them may be either cured, so far as we may determine this point clinically, or at least rendered free from symptoms by medical treatment. Those not faring so well may yet be subjected to exploration.

In general, ulcers showing the roentgenological signs of a protected perforation present such extensive adhesions and such crippling of the motor functions of the stomach that I have commonly assigned them at once to the surgeon.

In case of ulcer at or near the pylorus, of long standing and with marked food retention, Sippy claims entire cure in many cases by medical treatment. Provided the cicatricial contraction be not extreme, and that adhesions be trivial, we may grant this claim in many cases. There should be, in my opinion, no objection to a trial of medical treatment, but the improvement should be fairly prompt and decisive, as, fortunately, it generally is. The dangers of permanent pyloric blocking must not be overlooked, nor the chance of later hourglass stomach, nor the more tragic development of malignancy, which we so often find in these cases.

I think much more latitude is to be allowed in the use of medical treatment, in case of gastric ulcer, than in that of the duodenal type. The results of medical treatment in the latter, in my experience, have been much less certain, and the dangers of hemorrhage and of perforation much more to be feared. On the other hand, the lessened likelihood of cancer is to be given due weight in the decision.

To some extent the social status of the patient may influence us. If the subject must work daily for a living, the need of an attempt to secure a prompt and complete cure may decide us in favor of surgical intervention, while those who can afford to spend most of their time and much of their energy in nursing a diseased stomach may at least postpone such a course.

In general, we may mention as *advantages of medical treatment:*

1. Avoidance of immediate operative and anesthetic dangers. As in many other problems of life, certain individuals prefer to take years of lesser risk than hours of greater hazard. In no patients do we see better illustrations of this tendency than in those with peptic ulcer.

2. Avoidance of danger of occurrence of "vicious circle," later jejunal ulcer, postoperative adhesions, ventral hernia, etc.

3. In many cases, an advantage of medical treatment lies in the fact that work may often be continued at least in part during the medication.

4. Avoidance of the postoperative pain and abdominal distress appeals to many sensitive patients with peculiar force in favor of the medical treatment.

Next, we may speak of the *advantages of surgical treatment:*

1. We should place first the overwhelming advantage of knowing precisely what we are treating. This factor should not be estimated too lightly by the therapeutic enthusiast, for all who have seen many of these cases upon the operating table can recall instances of supposed ulcer in which no ulcer existed, but in which the symptoms were due to chronic appendicitis, to gallstones, to adhesions about the gallbladder, to Treitz's hernia, to kinking of the duodenum because of anatomical aberrations, to adhesion of the gastric wall to the abdominal parietes at the site of a long-healed ulcer, etc. I think it is within the bounds of prudence to state that, in a very material proportion of the cases of ulcer and supposed ulcer coming to operation, even when they have been in the hands of the most eminent men of the profession, such failures of exact diagnosis are discovered and always will be discovered, since they are oftentimes wholly unavoidable even with the most intelligent use of all our present means of diagnosis. In other words, we may often determine very definitely that a lesion of some type exists, interfering seriously with gastric function, but the exact character of the lesion may not be susceptible of diagnosis. In this connection I quote from a previous paper:

"There are certain unusual conditions within the abdomen incapable of preoperative diagnosis, so far as I know, which may simulate ulcer so closely that years of medical treatment are submitted to in certain instances. Thus I have encountered pinching of the pylorus and duodenum in Treitz's hernia, as mentioned above; compression of the duodenum by the superior mesenteric vessels, with dilatation of its proximal portion; kinking of the viscus by adhesions about the gallbladder and pressure on it by gallstone, and distortion from various causes, bringing about partial obstruction. In some of these cases the diagnosis of ulcer seemed to rest on a solid foundation, since pain, hyperacidity, vomiting, hematemesis, dilatation of the stomach, rigidity and tenderness were present, but medical treatment was of little or no avail in any."

I have records of three cases, all treated for a time as ulcer, and in my opinion extremely difficult to differentiate from this condition. Yet all three were due to congenital anomaly in the position of the duo-

denum, and all were cured promptly by operation. It is a great advantage of surgical exploration that such a condition may be recognized and efficiently treated, while diagnosis is probably impossible by the usual clinical and roentgenological methods. Without giving the case histories, it will suffice to say that two of the patients had had the appendix removed without relief. All had the persistent sour stomach so commonly noted in ulcer. Two had daily and the third occasional vomiting. Hematemesis had occurred in one, and all three had long been confined to bed. Food relief was noted in one, and in one the stomach was much dilated. In all three marked tenderness and moderate rigidity were present at the epigastrium, and in all three a fairly high gastric acidity was found. In two of the cases complete relief was given by correction of the angulation of duodenum caused by its anomalous position, and in the third by gastroenterostomy.

Because of the infrequent recognition of these cases I think it well to offer in detail the anatomical findings as given me in two instances by Dr. Leonard Freeman, and in the third by Dr. C. E. Tennant:

Case I.—"The duodenum ran directly downward, beneath the transverse mesocolon; then turning to the left it passed under the superior mesenteric vessels, well below the mesocolon, and appeared upon the left aspect of the mesentery of the small bowel. A strong band of connective tissue from the mesentery dragged a loop of the first portion of the jejunum upward to a point just above the place of emergence of the duodenum, in such a manner as to sharply kink the bowel. Above this kink the duodenum was dilated, as was also the stomach to a moderate degree. The pyloric opening was unusually large."

Case II.—"The condition represented a well-marked congenital anomaly. The duodenum did not, as it normally should, pass above the colon and beneath the stomach and emerge into the free peritoneal cavity through the mesentery of the transverse colon to the left of the spinal column. Instead of this it ran directly downward and through the colonic mesentery to the right of the spine. It then turned squarely to the left, crossed the vertebræ beneath the superior mesenteric vessels, and was looped up by firm adhesions (Treitz's ligament) to the point where it normally should have emerged; thus kinking it acutely, like a rubber tube hung over a nail, and producing a partial obstruction which gave rise to stasis and to marked proximal dilatation."

Case III.—"The stomach was of normal size and position and there were no scars about the pylorus. The duodenum, however, was quite as large as the transverse colon, and the terminal portion did not make its exit through the fossa duodenojejunalis. After considerable search the jejunum was found lying directly over and to the right of the vertebral bodies and its anatomical relation to the superior mesenteric vessels much the same as when the ascending portion of the duodenum is at the fossa duodenojejunalis on the left side of the vertebral bodies. There seemed to be no undue constriction at the ligament of Treitz, which was transposed to the right side of the spine, but crossing the bodies of the vertebræ were the mesenteric vessels directly over the transverse portion of the duodenum. Assuming that this transposition of the terminal third of the duodenum was responsible for the dilatation of the duodenum and the persistent vomiting, a gastrojejunostomy was made."

In another case, which had recently been subjected to a prolonged course of antisyphilitic treatment by a genito-urinary surgeon, the supposed ulcer symptoms were found to be due to a gumma of the liver, with extensive adhesions at the exact site of the pain and tenderness.

2. The chance of finding incipient and curable cancer of the stomach by exploration when the diagnosis of ulcer is apparently well established, should not be forgotten. In 6.4 per cent. of my first 93 cases of ulcer coming to operation, reported in 1911, cancer was demonstrated. Enough cures may be obtained in these cases by radical surgical procedure wholly to offset perhaps the usual mortality of operative intervention.

3. Even if the diagnosis of ulcer has been correctly made, there are many chances that a complication, as for example, gallbladder disease, chronic appendicitis, Lane's kink, etc., may exist. Such complication is discoverable upon operation only, in many cases. I certainly think we are justified in taking the position that no medical treatment of gastric ulcer is justifiable in the average case if a definitely established chronic appendicitis is demonstrable. The ulcer may heal, but the same pyloric spasm and hyperacidity which resulted from the appendicael lesion, and which presumably caused the first ulcer, will probably cause a second one when the patient returns to his ordinary occupation and diet. The same reasoning should apply in case of many other complicating affections.

In one case a diagnosis was made of a previous ulcer, presumably healed, and of a new one at the pylorus. The scar of the former was found several inches from the pylorus, but the later symptoms were due to the intermittent pinching of the pylorus and duodenum in a Treitz's hernia, this being severe enough to cause hematemesis on several occasions. I do not think the differentiation from ulcer was possible, yet medical treatment would obviously have been futile.

4. The avoidance of many serious complications of ulcer should be credited upon the surgical side:

First, we should mention cancer, while less serious are permanent pyloric stenosis, extensive adhesions, gallbladder and pancreatic disease, hourglass stomach, perforation, hemorrhage, subphrenic abscess, and a whole train of complications which are worse than the original disease.

The danger of perforation is not to be disregarded. In my first 116 operated cases, 4 gastric and 4 duodenal ulcers perforated acutely. There were many instances of chronic perforation, so often indistinguishable from simple adhesions that the exact number cannot be stated.

The frequency and gravity of hourglass stomach from chronic ulcer must not be underestimated. This complication was present in 5 of the 116 cases above quoted, the stomach being trilocular in one instance.

5. Operation often enables us to remedy some annoying trouble which, in case of a so-called medical cure, will persist and render the patient a semi-invalid. As an example I will mention the small omental hernia so frequently found associated with peptic ulcer, and so often overlooked. It not infrequently causes as much distress as the ulcer, and is probably to some extent a causative factor in some cases. Adhesions to the anterior abdominal wall often occur, and after ulcer is healed still cause much distress.

6. By operation we occasionally preserve the patient from disaster by the avoidance of perforation, which we find imminent when the abdomen is opened. I have several times seen the peritoneal surface over the ulcer already covered with flakes of lymph. The difference between the light mortality of simple gastroenterostomy in such cases with repair of the ulcer and that after perforation has occurred, is to be considered.

7. In lingering cases the advantage of the decisiveness of surgical procedure contrasted with the long-drawn-out course of medical treatment is to be properly estimated.

The *disadvantages of medical treatment* may be mentioned as follows:

1. Uncertainty of diagnosis, as already mentioned. Let no one underestimate the danger of incorrect or incomplete diagnosis in these cases, no matter how skilful the attendant. One of Leube's supposed ulcers recovered promptly after 25 years of suffering when his appendix was removed, under my care, and the stomach was found entirely normal. I have seen a score of more or less similar cases.

2. Frequent complete failure of medical treatment.

3. Likelihood of relapse. Probably more cases relapse than remain well, if they return to the usual habits of life. This certainly does not hold in cases well treated surgically, so far as my observation goes.

4. Danger of hemorrhage and perforation. We may hope to dismiss these dangers, after operation, in nearly all cases.

5. Fear of development, of the invalid habit, of chronic nervous prostration, chronic nephritis, arteriosclerosis, generally lowered resistance, with tendency to the development of tuberculosis or other chronic disease. The danger of the morphine habit is appreciable.

6. Under medical treatment we have the constant fear that malignant disease may develop. The presence of a high gastric acidity is not to be taken as evidence that cancer does not already exist, as I have learned to my sorrow.

7. The complications heretofore mentioned, and embolism, thrombosis, parotitis, phlebitis, etc., are too frequently encountered under medical treatment. We may repeat here that nearly all the mortality in peptic ulcer comes in some way from some complication. Obstruction by the ulcer, or by adhesions, of the biliary and pancreatic ducts is a serious possibility.

8. There are, unfortunately, many instances of subphrenic abscess, empyema, pyopneumothorax, septic pericarditis, mediastinitis, etc., which result as late complications of slowly perforating ulcers, their origin often wholly unrecognized.

Disadvantages of surgical treatment:

1. Danger of operation and of anesthetic. In good hands the mortality of perhaps one to three per cent., considering the seriousness of the disease under treatment, is to be regarded as justifiable.

2. Subsequent development of adhesions, vicious circle, jejunal ulcer, etc. These dangers are much lessened under modern surgical measures.

Gastrojejunal ulcers are generally conceded to be surgical, since they are so commonly dependent upon the use at the performance of the gastroenterostomy of a non-absorbable suture material which fails to come away. The less frequent jejunal ulcers are more amenable to medical treatment.

We should, then, weigh carefully the matter of the certainty of the diagnosis, the probability of relief by medical treatment, or of complete cure in favorable cases, the chances of relapse, the favorable or unfavorable physical condition of the patient, the danger of cancer, the possibility of relieving some complicating trouble by operation, the favorable or unfavorable occupation and surroundings of the patient, and, to some extent, the patient's desires. There should be no bias in the medical mind in favor of one line of treatment or another, excepting as it is based upon all of the above considerations.

DIGITALIS IN THE TREATMENT OF AURICULAR FIBRILLATION; AND A REPORT OF THREE CASES OF ARRHYTHMIA

BY HERMON C. GORDINIER, M.D.,

TROY, N. Y.

The object of this communication is to discuss the value of digitalis in the treatment of auricular fibrillation and to record three interesting cases of arrhythmia occurring during the course of acute infectious fevers. The diagnosis of auricular fibrillation is, for the most part, comparatively simple, the gross irregularity of the ventricular action being indicated at the wrist in a decided difference between each beat as regards tension, volume, spacing, and timing, while at the heart the tumultuous irregularity of ventricular action is easily discerned with the ear or stethoscope applied to the impulse. This irregularity of the arterial pulse taken in conjunction with the presence of a definite deficit or incongruity between the rate of the clinical apex and that of the radial artery, the radial rate being much slower than that of the apex, makes the diagnosis almost positive. In cases of fibrillation coming on rather abruptly in individuals suffering with mitral stenosis, the disappearance of the characteristic crescendo type of presystolic murmur and the equally characteristic thrill, and their replacement by a murmur softer in quality and generally long drawn out occupying the entire diastole, or mid-diastolic in time, and unaccompanied by a thrill, are also highly suggestive, if not absolutely diagnostic, of this condition. As before mentioned, in cases of fibrillation with mitral stenosis, where the fibrillation is of short duration, as it disappears and normal auricular activity is reestablished, one is able to note by auscultation the reappearance of the previously lost presystolic murmur, and to palpate the returning strictly localized presystolic thrill. These signs are ordinarily quite sufficient to establish the diagnosis of auricular fibrillation. They may be corroborated, however, by taking short stretches of polygraphic or electro cardiographic curves, when the disappearance of auricular activity and the presence of fibrillation will be indicated by the absence of the "A" wave in the phlebo- and cardiogram and the "P" variation in the electrocardiograms, and the appearance of a true systolic venous pulse in the jugulars, and in tracings obtained from the pulsating liver, together with the presence of multiple wavelets of small amplitude in the diastolic period of tracings taken from the jugulars and apex and in the electrocardiograms. Clinical alternation is sometimes

mistaken for fibrillation, inasmuch as in some cases of alteration the rhythmical irregularity in volume, so characteristic of the arterial pulse, creates waves so small in amplitude that the palpating finger fails to appreciate the difference in volume, and hence they are confused with the pulse irregularity of cases of fibrillation. Careful blood pressure observations or short strips of radial curves will dispel all doubt as to their true nature, as the radiograms in alternation show well-formed waves of large and small amplitude following each other in regular succession, the spacing between them being about equi-distant, or the long time interval existing between waves of long and small amplitude rather than as in ventricular extrasystoles between the small and large waves. Blood pressure studies show in alternation a halving of the radial rate on the side of the compressed arm at the height of the systolic pressure, whereas when the pressure of the cuff is released both large and small waves pass through when the radial rate becomes the same in each wrist.

From the standpoint of prognosis and treatment the recognition of the inception of this abnormal rhythm is of great importance, for it is nearly always associated with grave changes of the myocardium, and its presence adds greatly to the load of an already overburdened heart, whose reserve is thereby made more or less limited, both by increasing its irritability and conductivity, and by impairing its contractility, and thus diminishing its tonicity. While a few subjects of auricular fibrillation whose ventricular rates are moderately slow, and whose cardiac reserve is not greatly impaired, may live fairly comfortable for months or years, the great majority in whom this rhythm is perpetual are short-lived. Ventricular rates which are maintained above 120, unless responsive to proper therapy, go on to gradual or speedy cardiac exhaustion, with great dilatation and all the concomitant symptoms of an unrelieved decompensation and death. It is probable that the immediate cause of death in many of these cases is asystole, from the sudden inception of ventricular fibrillation. In determining the prognosis in a given case of auricular fibrillation it is therefore necessary to weigh carefully the subjective and objective symptoms, as well as to have a proper appreciation of the extent of the damage to the heart muscle—as indicated by the deficit between the rate of the apex and that of the radial artery; the amount of cardiac dilatation; the change in the quality and pitch of the heart sounds; and associated valvular murmurs, as well as to the condition of the arteries and functional capacity of the kidneys, and the ability of the heart muscle to respond to active digitalis therapy.

Recognizing keenly the import of the myocardium in maintaining the circulation, and the rôle its exhausted fibers play in the production of heart failure, I would state that no form of cardiac disorder is more amenable to proper digitalis medication than the one before us for dis-

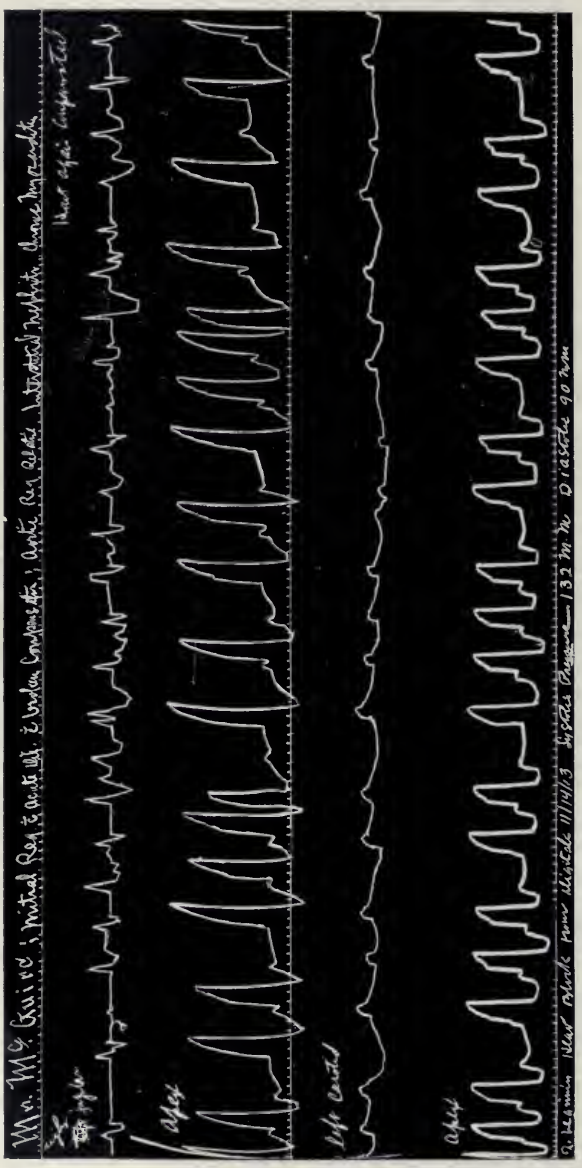

FIG. 1.—Auricular fibrillation, delayed conductivity, and occasional dropped beat due to digitalis. Note the widened A-C interval in the phlebogram and A-V interval in the cardiogram.

cussion. If we will pause for a moment to review the salient features of this disordered cardiac mechanism, we shall find ample justification for the above statement, for with the inception of this abnormal rhythm the coordinate auricular activity is lost and the whole ventricular myocardium is rendered more irritable from over-excitability, the result of innumerable stimuli constantly flowing from the auricles to the ventricles over His's bundle, the result of their delirious activity. This con-

stant increased conductivity rapidly exhausts the two most important functions of the heart muscle—contractility and tonicity—resulting in a most bizarre ventricular irregularity with dilatation of their chambers and myocardial exhaustion. We have been taught by both animal experiments and clinical studies that digitalis reduces cardiac rate by vagus stimulation through its effects on the cardio-inhibitory centers in the oblongata, as this action may be prohibited by blocking the vagus impulses to the heart through the administration of atropine. It has also been known for long that this drug has a selective action directly on the muscle fibers of the heart independent of their nerve supply, improving in marked degree the functions of contractility and tonicity. In addition we know from polygraphic and electrocardiographic studies that one of the earliest effects of digitalis is to delay conductivity through the bundle of His by increasing the auriculo-ventricular interval, causing, if the action is pushed, definite heart block, which effect is especially pronounced in cases where the bundle of His and the conducting system of fibers are diseased. This action of the drug is valuable in fibrillation by reducing the number of impulses flowing from the auricles to the ventricles, thus relieving their irregularity, slowing their rate and increasing their period of diastolic rest, thereby permitting a proper filling of the ventricular chambers. It also strengthens their systolic contractions, thus relieving them of their residual blood by increasing the volume output of the ventricles, with in most instances complete relief of the general venous stasis and edema.

In laboratory animals and healthy men digitalis increases blood pressure by constricting the small arteries through vasoconstrictor influences. On diseased hearts, however, great discrepancy of opinion exists as to whether such pressure effects ever occur. Mackenzie's observations seem to show that medicinal doses of digitalis in auricular fibrillation have no effect on the musculature of the arterial walls. It seems, however, reasonable to believe, especially where fibrillation with edema and low blood pressure exists, that such results occur chiefly through its effect on improving the contractile force and tone of the heart muscle, and especially of the ventricles, thus increasing the systolic output, reducing thereby the size of the dilated chambers by relieving them of their residual blood, augmenting the aortic pressure, and permitting a better coronary arterial flow, hence improving the nutrition of the heart muscle. Its diuretic effect is not primarily renal but is doubtless due to its selective action in increasing the force and strength of the heart muscle, thus delivering to the kidneys a greater volume of arterial blood under higher pressure, relieving their venous stasis and the general edema by exciting active diuresis. Rarely do we observe marked diuresis in cases of fibrillation without edema. Clinical experience teaches that when an active standardized preparation of

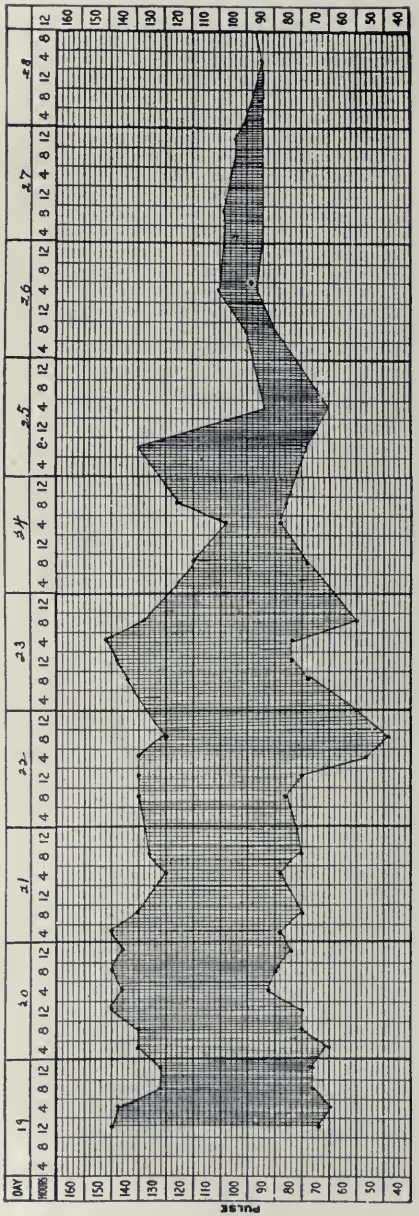

FIG. 2.—Pulse deficit chart. Record of auricular fibrillation showing marked myocardial exhaustion greatly improved by digitalis. The upper line is that of the apex rate, the lower of the radial rate; note the wide deficit at the onset and the gradual coalescence of the apex and radial rates under digitalis therapy.

digitalis fails to influence for good the strength of the myocardium, no increased urinary output occurs. Because of these well-known pharmacologic actions of the drug, we have in digitalis a most valued weapon whereby we may relieve and prolong the lives of these unfortunate patients, so that they may live months or years with comparative comfort, often being able to work at their usual vocations. The effects from

FIG. 3.—Case I. Mitral stenosis suffering with acute articular rheumatism, sudden onset of auricular flutter; radial rate, regular, 100; auricular rate, 300.

the use of digitalis or allied drugs in fibrillation are oftentimes no less than marvelous, patients in immediate peril of death being relieved as if by magic; the deficit between the rate of the cardiac impulse and radial artery gradually ceasing, the cyanosis dyspnea, and edema fast disappearing, the irregularity of rhythm and rapid rate quickly improving; and in cases of fibrillation associated with mitral stenosis the presystolic murmur long since absent, often reappearing with the improve-

ment of the functioning of the auricles. The drug to be effectual must be used at first in doses sufficiently large to produce its definite physiological effects—*i. e.* distinct lessening of the irregularity and slowing of the pulse rate, the rate of the apex and the radial pulse gradually becoming the same. When their rates reach seventy or under per minute it is wise to discontinue the drug for a few days, carefully watching the heart rate in the interval, and if it again becomes rapid, reaching ninety or more, then to give enough digitalis to keep it at about the normal rate, thus continuing the small tonic doses over long periods of time, only ceasing when the rate keeps normal and no deficit occurs between the apex beat and the radial pulse, or the drug produces some toxic effect, such as nausea, vomiting, diarrhea, severe headache, marked sinus irregularity, delayed conductivity, bigemina alternation or actual heart block. No drug of this series can, in my judgment, approach at all the good effects of an active preparation of digitalis if boldly pushed until its specific cardiac action is obtained. I would like to emphasize the importance of stopping digitalis therapy in cases of fibrillation immediately on the onset of bigemina or heart block. I am satisfied that the death of the patient of one of my colleagues with aortic disease was due to the lack of such warning. It is interesting here to note that the recent observations of Dr. Canby Robinson with lethal doses of digitalis on lower animals show that the first toxic change observed was a definite bigemina, soon to be followed by ventricular fibrillation and death. It is true that occasionally certain individuals seem to possess an idiosyncrasy for the drug and can take it neither by the mouth nor subcutaneously. In such patients the drug may be used intravenously or the substitution of strophanthus, ouabin, squills, convallaria, adonis, or spartein for a time may be tried. My preference is for either a good tincture, a perfectly fresh infusion made from carefully selected leaves, or recently collected dried and compressed leaves. In endeavoring to bring prominently before you the great value of this drug in the treatment of fibrillation, I do not wish in those cases of fibrillation with edema to underrate the great good that comes from absolute rest, restricted fluid intake, Karrel and salt-free diets, and careful elimination, or in combination with digitalis, of such diuretics that act upon healthy renal epithelium as the salines, caffeine, theobromine, or theocinsodium acetate. While these drugs often work admirably in conjunction with digitalis in the renal insufficiency of pure passive congestion, increasing diuresis and sodium chloride elimination, they are ofttimes disappointing and actually harmful in pure renal dropsy, particularly where the phthalein test shows a greatly reduced functional capacity. These latter drugs should not be given in pure renal dropsy. I want also here to emphasize the fact that belladonna or atropine should never be administered in this condition, unless for some very definite reason, such as

FIG. 4.—Case I. Auricular flutter transformed into digitalis bigemina under digitalis therapy for seventy-two hours.

the onset of a sudden fulminating attack of pulmonary edema, as its action is to paralyze the peripheral terminations of the vagus nerve, thus accentuating the fibrillation.

CASE I.—*Sudden Inception of Auricular Flutter During an Attack of Acute Rheumatic Fever, Transposed by Digitalis Into Continuous Bigemina and Then Normal Rhythm.*—The patient, Mrs. J. A. W., age 43 years, entered the Samaritan

Hospital, March 31, 1915, complaining of multiple joint pains aggravated by motion or any jar and severe sour sweats. Family history unimportant. Had measles, diphtheria, and rheumatism at 26 years of age; otherwise had been well until the onset three weeks ago of the present illness. She married at 23 years of age; has had one living child and one born dead at full term. Uses no alcoholic or other stimulants; denies venereal disease.

Present illness began three weeks ago with a severe attack of follicular tonsillitis, which confined her to bed for three weeks. Following this attack she developed pain and stiffness in her knees and wrists, which so disabled her that she sought relief by entering the hospital.

The patient is a well-nourished and developed female in the dorsal decubitus, and appears acutely ill. Both knee and wrist joints are red, swollen, and tender. The tonsils are enlarged, crypts patulous and they look diseased. The lungs show normal vesicular breathing.

The precordial region is not prominent. No retraction or Broadbent sign is present. No palpable friction rub. Localized to region of apex is a presystolic thrill. The apex is visible and palpable in the fifth interspace exactly intersecting the left midclavicular line. At this point and a little within is a strictly localized presystolic murmur of the crescendo type, ceasing suddenly with a slapping first sound to be followed by a systolic apical murmur, soft in quality and faintly conducted to the left. The pulmonic second sound is accentuated, but not reduplicated. No third sound or evidence of gallop exists. The radial and apex rates are 80 and perfectly regular in rhythm. Blood pressure: systolic 120, diastolic 80.

The spleen is not enlarged. Liver dullness extends from the fifth interspace to the costal border. It is not palpable because of the thick abdominal walls. The cranial nerves functionate normally. The reflexes, both superficial and deep, are normal.

The urine is dark amber, specific gravity 1022; contains small amount of albumin and a few hyaline casts. The blood shows a leucocytosis of 14,000; the blood Wassermann reaction is negative. The *x*-ray examination shows a moderate enlargement of the whole heart.

April 15, 1915.—About two weeks after the patient entered the hospital she was taken with dyspnea, rapid respirations, cyanosis, and orthopnea. The cardiac examination disclosed a rapid rate, the presystolic murmur and thrill were not discernible, the ventricular and radial rates were 100 and perfectly regular, while the auricular rate was 300. Polygraphic tracings were taken which confirmed the clinical diagnosis of auricular flutter. Digitalis therapy was instituted in doses of 20 minims of the tincture thrice daily. No change was noted in the flutter for 72 hours, when we were surpised to find that the flutter had been transposed into a continuous digitalis bigemina, rather than the usual sequence of fibrillation. This finding led to the discontinuance of the digitalis. A few days later the normal rhythm was again restored with a regular pulse both at apex and wrist at 70, with at the same time the return of the presystolic murmur and thrill. The patient remained in the hospital until June 1, 1915, and had no recurrence of the arrhythmia.

Case II.—*Sudden Onset of Auricular Fibrillation During an Attack of Grippe.*—Mrs. D., æt. 37 years, married. Entered the Samaritan Hospital, April 2, 1917, complaining of pains all over—headache, distressing unproductive cough, and sore throat. She was nauseated and had recurring chilly sensations.

Father died at 87 years of age of heart disease; mother died at 72 years of age of apoplexy; otherwise the family history is negative.

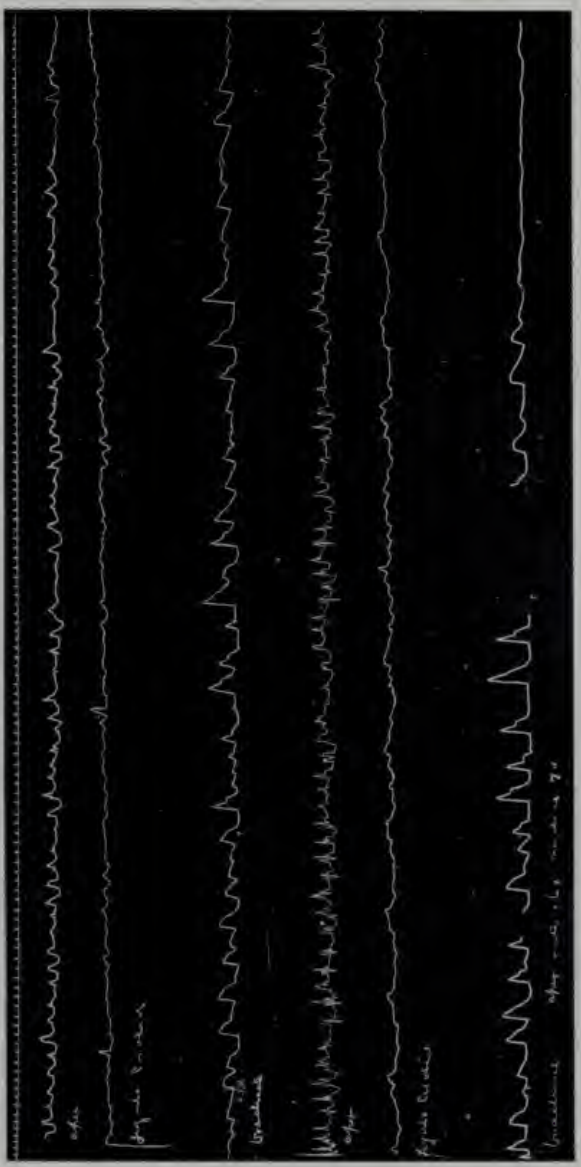

FIG. 5.—Case II. Auricular fibrillation occurring during an attack of grippe. Note the gross pulse irregularity and absent auricular wave in the cardiogram and phlebogram.

The patient had chorea at 12 years of age; pleurisy at 20 years of age. Four years ago she had quinsy. Otherwise she has always been healthy, save dyspnea on exertion. She has had three healthy children and two miscarriages. Denies venereal disease. She uses no alcoholics or drugs. She sleeps well; has a good appetite and the bowels are regular. She menstruates rather profusely. She had no knowledge that her heart was diseased.

Examination shows the patient to be poorly nourished, spare, and under-developed. Her expression is anxious. She is supported by three pillows. The skin and

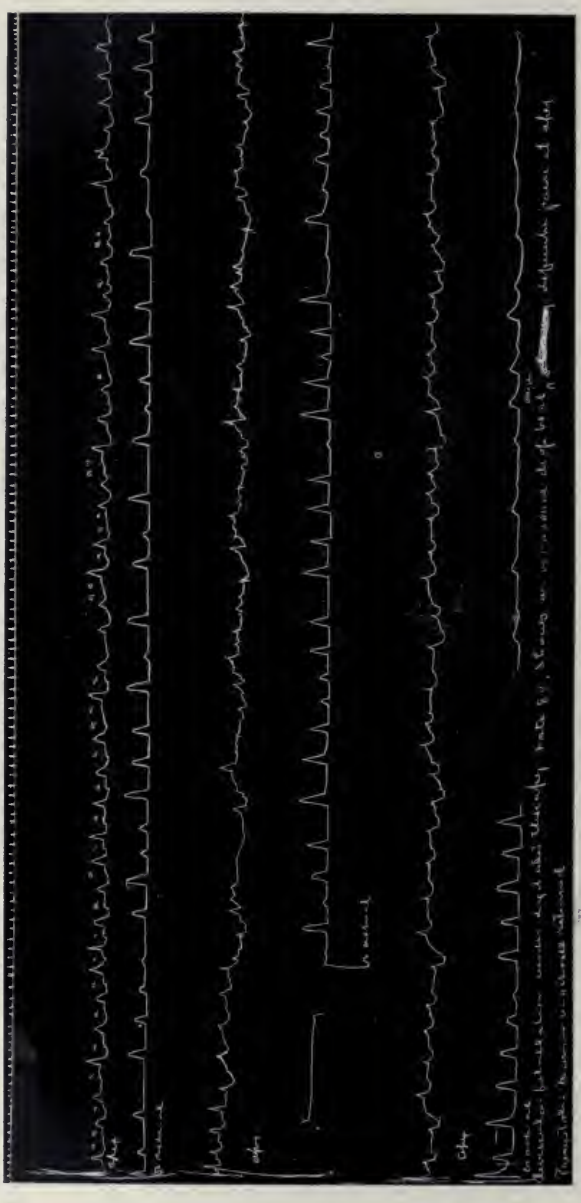

FIG. 6.—Same case as shown in Fig. 5 under digitalis medication. Note the recurrence of the auricular wavelets in the cardiogram, the widening of the A-V interval, the occasional occurrence of dropped beats—"2 to 1 heart block." The presystolic murmur and thrill have returned.

mucous surfaces are very pale. There is no edema or cyanosis. The respirations are quickened. The radial pulse rate is 80, and it is quite regular. A presystolic murmur and thrill are present. No deficit exists. The mucous surface of the throat is injected, tonsil enlarged, no exudate present. Dry and moist rales are heard throughout the lungs; otherwise chest is normal. The liver dullness extends from the fifth rib to costal margin; lower border smooth, not painful and not pulsatile.

Red blood count, 4,800,000; white blood count, 19,000; neutrophiles, 87 per cent.; eosinophiles, 1 per cent.; lymphocytes, 10 per cent.; transitional, 2 per cent.; hemo-

globin, 85 per cent. The urine is dark amber, acid, specific gravity 1,024, clear, albumin positive, sugar negative, red blood cells, hyaline and fine granular casts. Blood cultures show no growth on agar or bouillon in 48 hours.

On April 5, three days after admission and while her acute febrile symptoms were present, she suddenly appeared much worse; became distinctly cyanosed, had labored breathing, and complained of palpitation. She slept poorly. Examination disclosed an irregular pulse at 86 per minute, of feeble strength and volume, time, and spacing. The impulse was diffuse, apparently strong, irregular in force, and rapid, its rate being 158 per minute. The heart action was tumultuous and irregular; the presystolic murmur and thrill had disappeared. The jugulars stood out in bold relief and presented a large systolic venous movement. There was, as illustrated by the accompanying chart, a distinct pulse deficit. The cardiac dullness as outlined by percussion, showed the right border 4 cm. from the midsternal line and the left 13 cm. The upper border was at the lower border of the third rib. The polygraph showed the gross irregularity of the radial pulse, the large systolic venous movement with absence of the "A" waves both in the phlebo- and cardiogram. In all leads of the electrocardiogram the "P" waves were absent and fibrillating wavelets were present. She was given 20 minims of tr. digitalis every four hours, and after four days marked changes for the better were noted. Subjectively she was relieved of her dyspnea or air hunger, cyanosis, and insomnia; the urinary output was increased. The cardiac rate was slowed, the apex and radial rates fast approaching each other. The pulse was stronger, less irregular, and of greater volume. On the sixth day of digitalis medication the lost presystolic murmur and thrill reappeared, and tracings taken at that time showed in many cycles of the phlebo- and cardiograms returned "A" waves, with at the same time distinct diminution of conductivity with the occasional dropping out of beats; the latter also being appreciated on auscultation over the apex impulse.

She has gone on for a period of four weeks without the slightest discomfort, with practically no deficit between the apex and radial rate, and with a pulse of about 70 per minute, though still irregular. The presystolic murmur and thrill have remained and no edema has developed.

It seems probable that this case of acute fibrillation was induced through toxic changes of the heart muscles occasioned by the grippe infection, resulting in sudden dilatation with acute myocardial exhaustion. The good effect of rest and digitalis is noteworthy.

Case III.—*Recurring Syncopal Attacks Probably Due to Cerebral Anemia Occurring Toward the Close of the Convalescent Period of a Case of Severe Typhoid Fever, the Result of Auricular Flutter.*—Mr. John Y., æt. 35 years, entered the Samaritan Hospital, Jan. 28, 1917, in a delirious state, complaining at lucid intervals of severe headache, pain in the abdomen, and great weakness.

He was well nourished, without edema, his skin was hot and dry, pulse quickened but regular, tongue fissured, dry, and brown and sordes had collected on his gums, lips, and teeth. He talked incoherently, was disorientated and very stupid.

At the base of the right lung the physical signs of consolidation existed; elsewhere harsh but fair vesicular breathing was elicited.

The cardiac dullness was normal, sounds clear but distant, rhythm normal, rate 90. Blood pressure, systolic 120, diastolic 90.

Liver dullness extended from the fifth interspace to two centimeters below the costal border in the right mamillary line; the lower border was smooth and not tender.

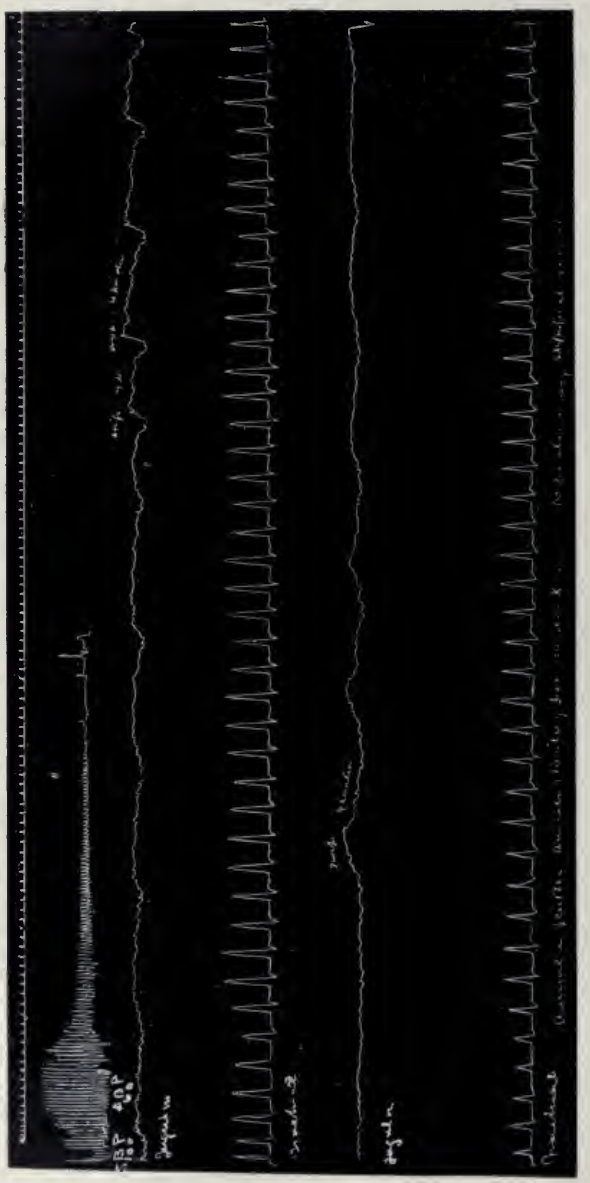

Fig. 7.—Case III. Auricular flutter occurring suddenly during convalescence from a very severe attack of typhoid fever. Auricular rate 300, radial rate 100. Normal rhythm was restored in five days with digitalis.

The spleen was palpable 2 cm. below the costal margin; it was definitely tender to the touch. The abdomen was universally tympanitic and distended; it was tender in the right lower quadrant. Rose spots were abundant on the abdomen and chest.

The pupils were mid-wide, equal, responsive to light and accommodation, the discs are normal. The patella and tendo-Achillis jerks were lively. The umbilical reflex was absent. The bladder and rectum were not controlled.

The urine was cloudy; specific gravity 1022; albumin in definite amount present; no sugar, leucocytes, erythrocytes, or bladder epithelium present; numerous motile

organisms were seen. The Widal agglutination test was positive; the Wassermann reaction negative. The red cell count was 3,250,000; the white cell count 5,200; hemoglobin 60 per cent.

The patient's temperature ranged for a period of about six weeks from 102° to 104°. During the third week of the disease he had three large intestinal hemorrhages which nearly cost him his life, but they were controlled, and though his condition was desperate for days he gradually improved. At the beginning of the seventh week he developed a sharp attack of facial erysipelas which was easily controlled with ichthyol. A few days later his temperature and pulse fell to the normal, his mind became clear, he appreciated his surroundings, and his appetite became ravenous. He was much emaciated, having lost thirty pounds in weight.

Suddenly while in recumbency he was taken with a faint attack, became very pale, the pupils were widely dilated, and his eyes were turned upward and outward under the cover of the upper lid. He was absolutely unconscious, but had neither muscular twitchings nor convulsions. The attack lasted about five minutes. When he returned to consciousness he was bewildered and disoriented, his pulse was rapid but regular, respirations quickened, and he was quite cyanosed. He had five attacks of a similar character during one week. I saw him in his last attack which was exactly similar to the one above described. His pulse was regular, feeble in volume, easily compressed, with the rate of 100; his jugulars were pulsating very rapidly, a series of fluttering wavelets which with a stop watch were counted at about 300 per minute. Polygraphic tracings were immediately taken which showed an auricular rate of 300, with regular rhythmic ventricular responses of 100 per minute, "3 to 1 heart block." His systolic blood pressure was 100 mm.Hg.; the diastolic 60. He was given 20 minims of tr. digitalis thrice daily for 6 days, when the normal rhythm was reestablished.

Three weeks later he was discharged, having had in the interim no return of the flutter.

DISCUSSION.

Dr. Thomas E. Satterthwaite of New York, stated that the papers on Auricular Fibrillation would assist materially in working out some of the unsolved problems of this affection.

So far as electrocardiograms and ordinary polygrams were concerned there were advantages in using both, because each either supplemented or confirmed the findings of the other. And yet in ordinary practice pronounced auricular anomalies could often be detected by the finger on the jugular. This fact he believed was not generally known.

In instances, however, where little fibrillation or flutter had developed or they were imperfectly marked an electrocardiograms or polygrams or both, would be desirable.

As the prolonged or continuous use of digitalis was indicated in auricular diseases, one could not be too particular in selecting a preparation of known strength that would be well borne by the stomach. It was well established that Tinctures of Digitalis, as dispensed in ordinary drug stores are of varying strength, and are not as well borne by the stomach as active principles of this drug.

THE PATHOLOGICAL PHYSIOLOGY OF THE HEART AS REVEALED BY THE POLYGRAPH AND THE ELECTROCARDIOGRAPH

BY LOUIS FAUGERES BISHOP, A.M., M.D.,

NEW YORK,

Clinical Professor of Heart and Circulatory Diseases, Fordham University School of Medicine, New York City; Physician to the Lincoln Hospital.

We all bow in admiration to the master minds of medicine who by ordinary signs and records have interpreted many diseases and processes and built up a very complete system of diagnosis. Accurate observation, both in the laboratory and the ward, must be intensively cultivated.

But it happens that many events in the circulation in well and sick people cannot be detected by the unaided senses. Consequently, the introduction of instrumental methods has contributed a vast sum of knowledge in a most important field of practice. Hence a meeting of the Section on Pathology and Physiology would be incomplete indeed at the present time if it did not at least illustrate and enumerate the achievements of this new science, which was opened for the first time to the profession at large, but not to laboratory workers, by the publication of Mackenzie's great work on the heart in 1908.

I remember very distinctly the satisfaction of understanding, in a measure, for the first time, after reading Mackenzie on the nature of the condition then known as "nodal rhythm," and now known as auricular fibrillation; then the gradual elucidation of one irregularity after another through the past decade, as the Mackenzie polygraph, and later the electrocardiograph, furnished the definite records on which to classify cases.

In this science of abnormal myocardial function, the physicist, physiologist, and the pathologist, meet in close cooperation. The physicist supplies us with the instruments and teaches us the laws that govern the mechanical activities; the physiologist points out the healthful action of the organ, and the pathologist its disorders.

There is no more remarkable example of the application of physics to medicine than the electrocardiograph. This instrument is a string galvanometer, and a good brief description is found in Lewis' "Clinical Electrocardiography." He describes it nearly as follows: The instrument which is described is known as a "string galvanometer," the

invention of Einthoven, a Dutch physiologist. It consists essentially of a powerful electromagnet, the poles of which are closely approximated; and of an extremely delicate conducting fiber of silvered quartz or glass which is stretched in the narrow gap between the two magnetic poles. If minute currents are led through this fiber as it lies in the magnetic field, the fiber moves in response to the tested current in a plain at right angles to the lines of magnetic force across the gap. The magnified shadow of the fiber is vertical, and is projected by means of an optical system and powerful light onto the horizontal slit of a camera; the shadow moves at right angles to and across the slit, and the movements are photographed on a sensitive film which travels behind the slit. The galvanometer is now made in New York City, and is a very serviceable instrument.

In practice, an electrode is attached to the right arm, the left arm, and the left leg of the patient, and a record is made of the three combinations that are possible in such an arrangement, namely: from the right arm to the left arm; from the right arm to the left leg; and from the left arm to the left leg. These are known respectively as Leads I, II and III.

The other instrument, which I am able to bring with me and show you, has contributed perhaps more to the knowledge of irregularities even than the electrocardiograph because of its wider distribution in use, and is known as the Mackenzie ink polygraph. To illustrate its universal applicability I show you over 2,500 tracings taken in actual clinical work. The movements due to the circulation are conveyed by means of a tube containing air, and registered by a tambour on which the lever rests.

The excursions of the lever are recorded on a moving strip of paper by pens moistened in ink. Of course, the instrument contains a clockwork arrangement for moving the paper, a time marker which marks dots at intervals of one-fifth of a second, and a special arrangement for getting the radial pulse. The instrument when once adjusted to the wrist and to the neck gives a simultaneous record of the wave motions in radial artery and jugular vein, and the observations can be continued as long as desired, which is very valuable when the heart only misbehaves once in a while and we want to know what the nature of the disorder is.

The pathological physiology of the heart, as revealed by the polygraph and electrocardiograph, has been classified into seven particular types of disorder. These types, as is true of all diseases, often merge one into the other, and two may be present at the same time. They are: (1) Sinus arrhythmia, (2) heart block, (3) premature contractions, (4) simple paroxysmal tachycardia, (5) auricular flutter, (6) auricular fibrillation, (7) alternation of the pulse.

Had this been a clinical meeting, it would have been a simple matter in this great city to have had examples of all these disorders before you.

Sinus arrhythmia is chiefly important because it is not of serious importance, and occurs as a physiological phenomenon in young children. It can be reproduced at any time in comparatively young people by taking a long breath. It consists of a difference in the length of the interval between the beats. When exaggerated in children it has sometimes led to the suspicion of myocarditis, and the children have been treated as invalids when they should have been playing out of doors. That can no longer happen under the advice of those who understand the use and interpretation of the polygraph.

The impulse of the heart ordinarily begins in the auricle and is transmitted later to the ventricle, so we have the auricle and ventricle contracting in rhythmic succession. If disease destroys the muscular contiguity or conductivity, we have the auricle and ventricle out of relation to each other. This has received the name of heart block, and is beautifully shown by the instrument described above, and it is due to this instrument that our knowledge of this condition exists.

In many people suffering from disturbed metabolism we find the heart apparently missing an occasional beat. The fact is, however, that the heart is not, as a rule, missing a beat, but the beat is occurring prematurely, and may pass unnoticed, while the succeeding beat is very large, and emphasizes the length of the quiet interval. This is called premature contraction.

When for any reason the heart abruptly becomes very rapid for a period and suddenly ceases to be rapid, we say that the person is suffering from paroxysmal tachycardia. This has been a most difficult field of investigation, and is still the ground of many disputed points. However, our instruments have disproved many previously held beliefs and pointed out not a few new facts.

One of the most recently recognized conditions is the extremely rapid though regular auricle, usually 250 to 300 per minute. It is always revealed by the electrocardiograph and occasionally by the polygraph.

The knowledge of auricular fibrillation is one of the most important contributions of clinical medicine that has come from the student of pathological physiology. In this condition there is a trembling palsy of the auricle, which transmits a vast number of impulses to the ventricle, and the ventricle becomes very rapid and irregular. It is the disease that yields most strikingly to the use of digitalis.

Alternation of the heart can be detected in many instances only by the polygraph. It is of extreme importance because it is a striking evidence of failure of the heart muscle. It consists of an alternation in the size of the beats.

These seven varieties of disorders of the heart beat have been

worked out by the use of these instruments and found the groundwork of our analysis of living pathological hearts. It is indeed a most beautiful and interesting study, and I should be most happy to have any of the members of the association visit my cardiac laboratory at any time during the meeting and take part in the use of these instruments and examine the records.

DISCUSSION ON PAPERS BY DRS. GORDINIER AND BISHOP.

Dr. Thomas Francis Reilly of New York, said he would like to insist upon a consideration of the Therapeutic side as well as of the other side. He believed that the results of the dosage of digitalis as described depended upon whether we were dealing with Hospital Patients or with those in Private practice, and he took it that Dr. Osborne was dealing with the management of cases as seen in private practice. If five or ten minims of tincture of digitalis were given, T. I. D., in such cases it might do good, but personally he believes in large doses, say ½ drachm or more repeated frequently until digitalization and then just enough to keep the pulse below 90. It was wonderful then how digitalis would carry them through. Personally he had never seen any value in the administration of sparteine or similar agents. When digitalis fails strophanthus and the rest of the cardiants commonly are worthless. When the abdomen was filled with fluid, apocynum occasionally works very well when digitalis fails. The dropsy disappears and the abdomen goes down. Apocynum had been called *"The Vegetable Trocar."* It is a gastric irritant and is frequently vomited.

Dr. Charles D. Aaron of Detroit.—He said that during the past year he has had gratifying results in cases suffering from hypertension by the application of duodenal lavage. In every case there was a clinical improvement. He reported the case of a woman, 45 years old, who suffered from dyspnea and high blood pressure. Sixty to ninety grams of magnesium sulphate in one liter of water was introduced into the duodenum through the duodenal tube daily and later twice a week. In the course of six weeks the systolic pressure fell from 185 to 165.

Dr. O. T. Osborne, of New Haven, Connecticut, said he was more than pleased with what had been said in regard to the great value of digitalis. There is no drug that equals digitalis in its action on the heart, and a fresh infusion or a good tincture represents the activities of the drug. The dosage of any one preparation must be determined by its action on the patient. He did not believe that in auricular fibrillation very large doses of digitalis should be immediately given, as he deemed it no more wise to suddenly over-stimulate a heart with this drug than it would be to plunge any muscle of the body into sturdy athletics without previous training. Therefore, he believed in beginning with small doses and either gradually, or if necessary more or less rapidly, increasing the dose. As soon as the heart's action was improved, and the digitalis action was thoroughly in evidence, the drug should not be given more than once in twenty-four hours.

The danger from digitalis in causing sudden death, especially in pneumonia, perhaps complicated with heart disability, should be recognized. Also, digitalis could cause death in heart lesions of various kinds. This cause of death is not often recognized, but is generally laid to the primary disease, or is termed a heart death.

The management of blood pressure abnormality is a subject for careful decision. A systolic pressure down to 105, with a diastolic of 85 certainly calls for treatment. A systolic of 260 or more and a diastolic of 160 or more, certainly shows a serious condition, and he has seen many such instances where repeated examinations of the

kidneys have shown the excretion to be absolutely normal. Also, in many such cases there is no organ of the body, apparently, abnormal. These instances must then be due to disturbances of some internal secretion. Radical changes in diet, hygiene and exercise have not affected these blood-pressures. Thyroid treatment is very valuable, and nitroglycerin, a drug whose lasting effect is laughed at by the laboratory men, shows positive activity in clinical cases, and the repetition of a proper dose of nitroglycerin three or four times in twenty-four hours shows a positive lowering of the blood-pressure almost invariably, unless there is nephritis.

Dr. Edward E. Cornwall, of Brooklyn.—The management of high blood pressure cases depends on what high blood pressure is. We may safely assume that whatever the circulatory apparatus does is done in the interests of an adequate circulation, and high blood pressure consequently appears as a manifestation of compensatory activity to meet some abnormal demand of the circulation. With the understanding that it is physiological instead of pathological, its regular treatment is limited to removing or alleviating as far as possible the conditions which make it necessary. This, in practice, consists to a very large extent in lessening the metabolic burden of the body by regulation of the diet; and the regulation which seems to be most effective is along the lines of reducing the quantity of the poisons produced in the alimentary canal from animal flesh by bacteria; which is done by giving a diet which is very largely lactovegetarian. Other dietetic considerations enter. Such regulation of the diet is the most effective thing we can do to bring about a reduction of the blood pressure in cases of persistent hypertension, and it is one of the satisfactions of the practice of medicine to see a steady and considerable decline in the blood pressure after adoption of such a diet. There are, of course, some cases in which the blood pressure is temporarily dangerously high, in which nature, in the presence of an insuperable obstacle, has lost her head, so to speak, and continues to raise the blood pressure higher and higher in the desperate attempt to relieve a hopeless situation. Then, to save the circulatory apparatus from immediate damage, it may be necessary temporarily to administer arteriodilator drugs which directly lower the blood pressure, but this is not very often required. The routine use of direct means to lower the blood pressure is wrong.

PRACTICAL POINTS IN THE USE OF STROPHANTHUS

BY EDWARD E. CORNWALL, M.D., F.A.C.P.,

BROOKLYN, N. Y.

The rise of strophanthus in the general esteem of the medical profession was slow until recent years, when the introduction of strophanthin made it easy to demonstrate its extraordinary power as a heart stimulant. Boos says of strophanthin: "It is the one active principle of the digitalis group which approximates most closely in its action to the effects of the combined digitalis bodies as they occur in the leaves."

The preparations of strophanthus which need be considered are the tincture and strophanthin. The tincture was once said to be unreliable, and most writers on strophanthus have repeated the assertion; and more recently it has been stated as a partial explanation of this alleged unreliability, that the active principles are changed in the alimentary tract so that they lose part of their efficacy. This assertion has not received confirmation in the author's clinical experience of many years with this preparation. If unsatisfactory results have been obtained with the tincture, a possible explanation may lie in the fact that it is generally given in too large doses. There seems to be no reason for believing that the tincture of strophanthus is less reliable than the tincture of digitalis, or other vegetable tinctures.

Strophanthin is defined in the Pharmacopeia as a mixture of glucosides derived from *Strophanthus kombé*. As offered by reliable drug houses it is derived from that and other varieties of strophanthus. The strophanthin derived from *Strophanthus gratus* is said to be identical with the exceedingly toxic ouabain, and has a different dosage from that of the *Kombé;* and these facts, as Satterthwaite has pointed out, make caution advisable in its use.

The dosage of the tincture which has been found most effective by the author is much smaller than that recommended by most of the textbooks and drug catalogues, which give the average dose at about 8 minims, (range 3 to 15 minims). The author's regular dosage is from one and a half to 3 minims, given every four hours. The regular dosage of strophanthin, as the author uses it, ranges from 1/1000 grain to 1/250 grain, given every four hours or less often. These doses of the strophanthin made by a well-known manufacturing drug firm, whose product is the one most used by the author at the present time, correspond to doses of the tincture of ¾ minim and 3 minims respectively, according to the statement of the manufacturers. Under certain conditions strophanthin

may be given in larger doses, even as large as 1/100 grain, but such large doses should not be repeated oftener than once in twenty-four hours; and doses of 1/250 grain should not be continued for long at the four hours interval, except in extreme cases.

The dose of strophanthin as given in the Pharmacopeia is 1/200 grain. The dose of Merck's strophanthin is stated to be from 1/320 grain to 1/60 grain. The dose of the Thomas-Merck strophanthin, which is made from *Strophanthus gratus,* is stated to be from 1/20 grain to 2/5 grain. The dose of the strophanthin of Burroughs, Welcome & Company is stated to be from 1/500 grain to 1/100 grain, the average dose being 1/200 grain. These doses are given for comparison with those mentioned in the preceding paragraph, which are the ones found most effective, as well as safe, by the author.

The tincture of strophanthus should be administered by mouth, well diluted with water. Strophanthin is best given hypodermically, sublingually or intravenously. The intravenous method is theoretically the best for quick effect, but is not always convenient, and requires strict precautions in its employment, for it possesses a certain amount of danger. The hypodermic method is generally to be recommended, because it combines effectiveness with convenience and safety, and is within the capacity of the nurse to carry out. The objection of Boos, that hypodermic administration of strophanthin "causes most intense pain and disturbance," is not borne out by the author's experience; at least, he has received few complaints from patients of pain, although not infrequently local irritation was complained of which, however, was usually slight. One patient, who received not less than three hypodermic injections of strophanthin daily during the past eleven months, has not shown any local disturbance or felt more than a tingling sensation from some of the injections. By injecting deeply the local irritation can be minimized. The sublingual method, in which a hypodermic tablet is placed under the tongue, dissolved, and absorbed, is a convenient one which does away with the hypodermic technique.

An idiosyncrasy in regard to the effects of strophanthus is sometimes observed when the drug is taken by mouth, and this manifests itself by nausea, anorexia, or, most frequently, by diarrhea. This idiosyncrasy is not observed often enough to make it necessary to consider these gastrointestinal symptoms as regular effects of the drug. In a case where the tincture given by mouth produced them, and where strophanthin given sublingually also produced them in slight degree, these symptoms were not observed by the author when strophanthin was given hypodermically.

The general indications for the use of strophanthus are those of a direct heart stimulant. In any cases where the systolic output requires to be increased, this drug may be used. In this field it competes with

digitalis, and, in the author's experience, has been found to have a wider range of applicability than digitalis. While in some cases of cardiac insufficiency, particularly those occurring in young adults with a comparatively healthy myocardium, digitalis may prove the more effective, the author has found strophanthus the more effective in all types of heart disease in children requiring a direct stimulant; also in mitral stenosis, in aortic incompetence, and in all cases where myocardial degeneration, acute or chronic, are present in notable degree. He has on many occasions given the two drugs for alternating periods of several days, and questioned the patient or nurse regarding the comparative results, and almost invariably the testimony has been in favor of strophanthus. Even in lost compensation from mitral incompetence in chronic valvular disease of inflammatory origin, which is considered the ideal field for the exhibition of the power of digitalis, the author has found strophanthus so effective and so free from unpleasant effects, administered in his preferred doses, that he has come to use it in that condition more or less regularly.

The contraindications to the use of strophanthus are not numerous. It is contraindicated in those cases where rest alone is sufficient to restore compensation. The gastrointestinal idiosyncrasy is a contraindication to its use by mouth, but not to the hypodermic administration of strophanthin. And it should not be given immediately after a strong course of digitalis.

Compare with these contraindications those of digitalis, viz.: ability of the heart to recover compensation by rest alone; childhood and old age; the existence of much myocardial degeneration, acute or chronic; acute endocarditis; mitral stenosis and usually aortic incompetence; atheromatous arteries; most conditions with high blood pressure; gastrointestinal irritation produced by its ingestion; its tendency to produce cumulative toxic effects; and its tendency to produce heart block.

On the other hand, strophanthus compares favorably with digitalis in the fact that it has few contraindications, and in the extent of its therapeutic range, and in that it has a special advantage in its freedom from cumulation.

Following are some accounts of the use of strophanthus in particular conditions, as the author has learned to use it.

In acute endocarditis and other acute inflammations of the heart with decompensation extensive enough to call for heart stimulation, tincture of strophanthus is given, usually in doses of two minims every four hours. In a child of three or four years, the usual dose is one-half minim and in older children, a minim or a minim and a half. In some forms of acute myocardial inflammation, notably diphtheretic myocarditis, the myocardium responds sluggishly to any heart stimulant, and the doses given may be a little larger than those mentioned

above. It is considered undesirable to give direct heart stimulants in cases of acute inflammation of the heart, but when there is definite and progressive cardiac insufficiency, they are required just as in other cases of cardiac insufficiency.

In typhoid fever with notable signs of myocardial degeneration, tincture of strophanthus is given in doses of two and a half minims every four hours. In cases of acute cardiac failure strophanthin is given in good-sized doses. The author has seen remarkable improvement follow the hypodermic injection of 1/500 grain of strophanthin in a suddenly developed dilatation of the heart in a typhoid patient, who had walked around with this disease for two weeks. This dose was continued every four hours for a few days, and then tincture of strophanthus was substituted in the doses above mentioned. The patient remained in bed for three months and made a good recovery.

In the author's plan of heart stimulation in pneumonia, strophanthus occupies the chief place. Ordinarily it is given in small or moderate doses, one and a half, two, two and a half, or, exceptionally, three minims of the tincture every four hours; and usually combined with strychnine sulphate in doses of one-sixtieth to one-thirtieth of a grain, every four hours. In extreme cases of myocardial failure, or in suddenly developed ones, strophanthin is given hypodermically, in doses of 1/500 grain, every four hours, or in a single dose of 1/100 grain or less. In an extreme case of cardiac failure, with a rapid and almost imperceptible pulse and extensive pulmonary edema, occurring in the fifth day of pneumonia, and apparently brought on by the fact that the patient got out of bed in delirium, the author has seen the hypodermic injection of 1/100 grain of strophanthin followed promptly by recovery of the heart to such an extent that the urgent symptoms cleared up, and the patient was able to go on to defervescence, which took place two days later. A physician of forty, who had shown symptoms of chronic myocardial degeneration for six months previous, developed pneumonia which extended over both left lobes, and in which the invading pneumococcus was identified as of type I (Cole's classification). The heart stimulation given throughout the active period of the disease consisted of strophanthin, 1/1000 grain, given hypodermically every four hours, with strychnine sulphate, 1/60 grain. On the eleventh day the patient defervesced by lysis.

In chronic valvular disease with decompensation of considerable degree, requiring direct heart stimulation, strophanthus tincture is given in doses of two or three minims every four hours, or strophanthin, 1/1000 grain, hypodermically, every four hours. In extreme decompensation in mitral stenosis, with auricular fibrillation, strophanthin is given hypodermically, every four hours, in doses of 1/500 grain, or even 1/250 grain, and usually morphine sulphate in combination with it in

doses sufficient to alleviate the dyspnea and restlessness. This combination of strophanthin and morphine has given the author the best results which he has been able to obtain in this class of cases. After securing compensation, which is often fragile, it may be necessary to keep up the administration of strophanthus in reduced doses, and sometimes of the morphine also.

In conditions of chronic myocardial degeneration with loss of compensation, strophanthus is employed when strychnine is not sufficient. Ambulant cases are given one or two minims of the tincture every four hours, and cases confined to bed, one to three minims every four hours. In the severe cases strophanthin is given alone or with morphine, in the manner before described. The superiority of strophanthus over digitalis nowhere appears more clearly than in the treatment of advanced chronic myocardial degeneration.

In conclusion, the author desires to emphasize this point in the use of strophanthus: that it should be used in the right doses, which, except when used for emergencies, or after establishment of tolerance, seem to be much smaller than those which have been generally recommended; for it is only by using it in the right doses that the best results can be obtained. There is reason to suspect that when given in excessive doses, especially if long continued, it can injure the heart, perhaps more than digitalis does.

THE ADULT THYMUS AND ITS TWO TYPES OF DYSFUNCTION

BY GEORGE HOWARD HOXIE, M.D.,

KANSAS CITY, MO.

The object of this paper is to show:

1. The importance of the thymus in endocrine upsets.
2. The two types of disturbance found in thymic dysfunction.
3. The localized pathologic conditions in the thymic area.

The thymus is a small mass of tissue lying in the anterior mediastinum. It is prominent in fetal life and infancy, and during that time may fill out the space between the trachea and the sternum and extend out well toward the carotids. In adult life one finds normally only shreds of tissue hanging down, as it were, from the level of the jugulum into the anterior mediastinum. These shreds in the living subject look like strings of fat and measure perhaps a half centimeter in diameter and two to four centimeters in length. They may lie against or behind the anterior edges of the pleurae; or, in hyperplasia, crowd the pleurae to the side.

The thymus originates from the third branchial pouches in early fetal life, and the two lateral halves grow forward and coalesce in the median line (in the third fetal month), sometimes retaining a connection with the thyroid above, sometimes retaining the connection with the fourth metamere. The coalescence in the median line is not complete, consequently the two parts develop independently and one lobe may develop out of proportion to the other.

They reach their greatest size between birth and 2 years of age. Then they remain more or less stationary until puberty, when atrophy sets in. But at no time do they quite disappear, for shreds of parenchyma can be found in the fatty tissues up into the seventh decade. Since the thymus is very sensitive to starvation and emaciation, it has been difficult to identify this tissue in the ordinary material of the morgue and dissecting room. Examples of the normal gland should be looked for only in the robust subjects dying from traumatism or very acute disorders.

HISTOLOGY

When examining normal thymus tissue under the microscope one notices first that there are lighter and darker areas, the difference seeming to be that the latter contain more lymphoid cells or lympho-

cytes. These areas are not sharply demarcated but seem to merge into one another. Further observation reveals a network of cells of the endothelial type among which the small round cells (or lymphocytes) seem congregated. Here and there one notices masses of distinct epithelial cells arranged concentrically—forming pearls, the so-called Hassall's bodies or corpuscles. Many cells have large bodies staining with eosin and reminding one of plasma cells.

Thymus tissue is differentiated from other lymphatic bodies in that it has a decided mixture of lymphatic and epithelial elements, whereas in the tonsils and adrenals, the epithelial elements are sharply separated from the lymphoid. It is differentiated from the lymph nodes in that it has no proliferation centers, no border sinus in the cortex and only the suggestion of a connective tissue framework (Matti).

The epithelial elements, the so-called reticulum cells, originate in situ, are fixed, and, although they react to injuries, are relatively stabile. The lymphoid elements (the so-called thymus lymphocytes) are derived from cells that have migrated into the thymus anlage. They are mobile and react vigorously in childhood to insults. In adult life they are usually of slight importance. They vary in number with the size of the body and also with its health and nutrition. The activity of the eosinophiles consists in storing up the active thymus secretion. That is, they are possibly the carriers of the hormone action of the gland. They are formed from the large reticulum cells. They are, therefore, a functional unit with the reticulum cells. Hart (Berlin) believes that the epithelial cells represent the real parenchyma of the organ and on them rests its activity. Therefore, the lymphocytes may be said to represent the condition of the body as a whole, and the epithelial cells that of the gland.

Hammar (quoted by Matti) gives the weight of the gland as set forth in the accompanying table. It is important to note that the weight of the parenchyma does not parallel that of the whole mass. These figures, of course, are illustrative rather than absolute, particularly with reference to adult conditions; for it is only of late years that thymus tissue is being watched out for and studied in routine post-mortems.

If we accept the experimental work of Klose and Matti it is evident that the gland has to do with calcium metabolism and forms a unit in the complicated interdependent pluriglandular system. For when the gland is removed in puppies one finds a dystrophy of the bones, and a hypertrophy of the spleen and adrenals. Since it atrophies when the sex glands begin to functionate, we infer that it is antagonistic to these glands.

HAMMAR'S FIGURES (MATTI)

Age	Gross Wt.	Net Wt. (Parenchyma)	Relation to Body Wt. Pro Mille
New-born	13.26	12.33	4.2
1- 5	22.98	19.26	2.2
6-10	26.10	22.08	1.2
11-15	37.52	25.10	0.9
16-20	25.58	12.71	0.5
21-25	24.73	4.95	0.4
26-35	19.87	3.87	0.3
36-45	16.27	2.89	0.3
46-55	12.87	1.48	0.2
56-65	16.08	0.73	0.3
66-75	6.00	0.03	0.3

HYPERTROPHY OF THE THYMUS

"There is a true persistence of the thymus and a true hyperplasia of the thymus, with which there appears often, perhaps always, not merely a hyperfunction but rather a dysfunction of the gland. They are the expression and some part of the phenomena of an abnormal constitution, of a disturbance of the equilibrium of the pluriglandular endocrine system, on which as a basis various disease-forms may develop. From the hyperplastic thymus a toxic influence seems to be exerted on the heart. The existence of a true status lymphaticus has not yet been proven with certainty. Rather it appears as if the swelling of the lymphatic apparatus represents a tissue reaction that is dependent upon the thymus and which can show itself in the lymphoid components of the thymus itself. Two sharply marked histologic types stand out: the so-called medullary hyperplasia, which represents a primary increase of the specific organ tissue; and a hyperplasia of both zones in nearly normal relations, which argues for a secondary increase of the nonspecific lymphoid elements of the gland in a (usually primary) hyperplastic thymus."—Hart, *Vichows Archiv,* Vol. 214, p. 82.

"Enlargement of the thymus gland may, in some cases, produce symptoms and physical signs closely resembling any form of tumor of the anterior mediastinum. Such a condition of affairs is rare, owing to the fetal character of the gland, but it has occurred in quite a number of cases. The causes for such a hypertrophy are not clearly known, and the treatment is equally unsatisfactory, while the differential diagnosis of this condition from other diseases of this space is virtually out of the question, unless percussion gives a dulness beginning high up in the neck and extending without a break down along the chest wall."—Hare, *Affections of the Mediastinum,* 1889, page 147.

The *symptoms* caused by hypertrophy of the thymus are in the child largely due to pressure. In the adult, on the other hand, the symptoms

are largely due to the chemical products of the reactivated glands.

In the child, therefore, we find a dyspnea of the obstructive type, with the child trying to relieve itself by tossing about and bending its neck in various directions. Such a dyspnea occurs frequently in the course of bacterial infections, particularly those in which the throat is involved. There is the sense of weight on the upper chest.

In the adult, on the other hand, the complaint is chiefly of weakness; of being short winded; of being unable to get a long and satisfying breath. The weakness is also evidenced in the abdominal area by complaints of flatulence, constipation and loss of appetite. The muscles seem fairly strong, but the patient finds himself unable to use them. Thus even walking is fatiguing.

In other words one has a picture of the conventional myasthenia gravis without the bulbar symptoms.

The family history of these patients, both infantile and adult, shows neurotic stigmata. Thus a child in my practice who was troubled by dyspnea in every attack of tonsillitis, measles, pertussis or similar trouble, dyspnea that was always accompanied by the submanubrial dulness, had a father who was afflicted with a psychopathic disorder so pronounced as to necessitate his being kept in an asylum for some time. Again the mother of another patient, an adult, had Glenard's disease. Whether such stigmata have any material force in the thymic disturbance is a question.

In the child the finding of submanubrial dulness should put one on guard. One should examine for an enlargement of the bronchial glands, especially by listening for an increase in the whispered voice along the spine down to the level of the scapular spine (d'Espine's sign). The extension downward of the normal area for hearing the whispered voice points to an enlargement of the bronchial glands rather than to that of the thymus. Anteriorly one is apt to hear a stridor over the manubrium from the compression of the trachea, if the thymus is enlarged. This is rarely the case when the bronchial glands are enlarged. The Roentgen ray should be used to verify the findings made by physical examination, and in the child the thymic shadows are so distinctive that little doubt need be entertained as to whether the gland is hypertrophied or not.

In the adult the conditions are more complicated. We must distinguish between (a) substernal thyroid, (b) enlarged aorta, or aneurysm, (c) peribronchial glands, (d) tumors of the mediastinum, and (e) reactivated thymus. Simple percussion is not sufficient to do this. The presence of d'Espine's sign would generally rule out thymic hypertrophy. Pulsation and thrills would also rule out the thymus. But this leaves most cases in doubt. Therefore, the Roentgen ray must be resorted to. The fluoroscope will determine whether the mass moves with the act of swallowing, thus identifying the thyroid. It will also

show pulsation, thus identifying arterial tumors. If the chest be viewed in the oblique position one can distinguish bronchial glands from the thymus—for the former fill up the clear space just in front of the spine. The fluoroscopic views should be verified by plates taken both in the anteroposterior and the right oblique planes.

The microscopic study of tissue removed at operation and postmortem has shown two general types or conditions. In the first, we find the lymphatic elements predominating; in the second, the epithelial. The first is found in the hyperplasia of childhood and in the hyperplasia accompanying septic or toxic disorders in the adult. The epithelial elements predominate wherever the history shows endocrine upsets, as in the reactivated thymus of the adult. The first makes itself known chiefly by its mechanical influence; the second by its chemical. We illustrate the first from a case of septic abortion; the second from a case of myasthenia. We might have chosen for the latter equally well a case of Graves' disease.

The treatment in the child is that of removal of the gland—or its destruction by means of the Roentgen ray.

In the adult we begin with the employment of the thyroid and sex glands in extract. If after a month's trial—coupled, of course, with bed rest and general treatment—no results are obtained, it is justifiable to resort to excision, or at least to heavy therapeutic doses of the Roentgen ray.

The dose of the thyroid extract varies from 1/5 to 2 grains, given on an empty stomach, at least 30 minutes before eating.

In females we now have good preparations of corpus luteum to add to the thyroid. In males we are not so fortunate, but now and then can find a good preparation of the testicular fluid. Of these preparations the dose is not yet well fixed and needs to be worked out in each case.

A good adjuvant for this medicinal treatment is arsenic administered with the needle. I prefer arsacetin in doses of 1.0 to 2.0 c.c. of a 10 per cent. solution. Sodium cacodylate may also be used in doses of 3 to 7 grains. I usually administer the arsenic every third day.

EXPERIENCES IN RECONSTRUCTIVE SURGERY OF THE EXTREMITIES

BY WAYNE BABCOCK, M.D., F.A.C.S.

Surgeon to the Samaritan, Garretson, and American Stomach Hospitals, Philadelphia.

In 1903, on assuming charge of the Surgical Department of the Samaritan Hospital, we were impressed by the large number of primary amputations performed in this service for injuries and infections of the hand. On inquiry it was found that there was a time-honored custom that resident physicians were permitted to have all amputations that did not involve tissues above the wrist or ankle, and that there was an active rivalry as to who should have the greatest number of these amputations. A rule was passed that no amputation of even a part of the finger should be performed without the explicit direction of one of the chiefs of the service. As a result, amputations involving the hand, in this service, have become, perhaps, somewhat rarer than amputations at the hip-joint, and there has been developed a pride as to the amount of tissue saved to the use of the patient rather than the height of amputations performed by the resident physicians.

In this service it is our rule to consider all tissue as viable until absolute necrosis is proved. Lack of primary vascularity after the injury is not considered evidence of the molecular death of tissue, and necrosis, even though extensive, in most cases is not considered an indication for amputation.

In the handling of injured hands and feet the following points deserve consideration.

1. The Determination and Maintenance of Viability of Tissue.—A portion of the hand or foot which is cold, without sensation, and which does not bleed on incision, may yet, under proper conditions, recover. As a rule, therefore, the part is placed under the best environment for the restoration of function until evidence of putrefaction proves that there is no hope of saving the tissue. Tissue that is partially viable when first seen may be destroyed by improper handling, especially in the first-aid treatment. For crushing and lacerating injuries, primary sutures should not be attempted: the parts should be cleansed, arranged upon a splint, and protected from tension or irritants, including the stronger antiseptics. The dressings should be voluminous, non-constricting, supportive, and continuously wet; and only after the circu-

lation has been thoroughly reëstablished, and there is evidence of the complete subsidence of any primary infection, should any attempt be made to unite the divided tissues. Not only should the injured part be put at rest, but if the injury is severe the patient should be kept in bed until all primary inflammatory symptoms have subsided.

It is important to remember that tissues primarily living may become necrotic from the tension resulting from secondary swelling. After a violent contusion of the hand or foot, the chief swelling comes from the overlying and relatively inelastic skin. One should determine, then, immediately after injury whether the secondary swelling will probably be such that the skin tension will arrest the blood and lymph circulation in the part, and, if such seems likely, long incisions should be made through the skin over the part contused. For example, for a crush of the forearm an anterior and posterior incision from the elbow to the wrist or fingers may be made. These very free longitudinal incisions will often prevent secondary destructive necrosis and infection, and enable the part to be saved. The three following outlines of cases illustrate the value of these methods in treatment:

Case I.—*Illustrating Harmfulness of Primary Suturing.* Crushing injury of the hand from the fall of iron casting treated by painstaking sutures of muscles and tendons and careful union of the overlying skin. Secondary disorganizing infection extending to the elbow and involving the tendons and bone. Final recovery without amputation, but with a seriously crippled and almost useless hand.

Case II.—*Illustrating Value of Rest and Wet Dressings for Pulpified Hand.* Disorganizing injury, with partial pulpification of tissue and multiple compound comminuted fractures, due to the passage of the hand between heavy cog-wheels. Hand considered to be disorganized and not viable, but treated by absolute rest, freedom from tension, and constant wet chloretone dressings. Healing with practically no suppuration or loss of tissue, and moderate deformity.

Case III.—*Illustrating Value of Free Skin Incisions in Terrific Crush of Forearm.* Disorganizing crush of the hand and forearm from being caught between the bumpers of a railroad train. Multiple compound comminuted fractures, marked primary swelling, and great tension from blood extravasation. Treated by long incisions from the elbow to the wrist or fingers, absolute rest, and constant wet applications. Loose fragments of bone laid in place and not removed. Wide separation of divided skin, but no secondary infection or loss of tissue. Recovery with a slightly bowed but very strong and useful hand and forearm.

2. Replacement of Amputated Parts.—Portions of tissue partially or completely detached by incised wounds may be replaced and lightly fixed in position by suture. But few sutures should be employed to avoid traumatism, constriction, or interference with drainage. If there

is an associated contusion or marked laceration, it is well to place no sutures through the skin, but simply to reaffix the part by a few fine sutures of chromic catgut or similar material, uniting the deeper muscular or aponeurotic planes only. By avoiding skin sutures better drainage is secured, constriction and swelling from secondary swelling is largely avoided, and there is a much better chance of saving the part. This is well illustrated in Case IV.

Case IV.—Extensive laceration and contusion with multiple fractures of the hand due to the explosion of a Fourth-of-July bomb in the hand. Thumb disarticulated at the carpometacarpal articulation and hanging by a narrow strip of skin with intra-articular fracture. Thumb replaced, fastened in position by sutures through the muscular tissues only, skin not sutured, continuous wet dressings. Primary union without suppuration or necrosis, with restoration of a somewhat shortened but useful thumb, having only slight limitation of movement.

3. Revitalization of Tissue by a New Source of Blood Supply.—With certain badly crushed, contused, or lacerated wounds of the hands or feet it is evident that a part has been cut off from its source of blood supply, while the proximal tissues are so devitalized as to prevent the regeneration of new blood-vessels until long after the terminal portion of the injured member has undergone necrosis. In such cases we have endeavored to obtain an immediate new source of blood supply for the preservation and rehabilitation of the damaged tissue by immediately burying the part in the anterior abdominal wall or elsewhere. To aid the process, median incisions on the dorsal and palmar surface of the fingers are made, the edges of skin turned back and held apart by sutures. In this way both the anterior and posterior surfaces of the affected fingers present wide, skin-free surfaces, into which, after imbedding, new capillaries may at once sprout. For disorganizing injuries of the foot we have buried the mutilated part under a skin-flap raised from the calf. Of the four cases in which we have tried this method, in three we were able, we believe, to save tissue that otherwise would have been lost, while in the fourth the mangled tissues of the hand underwent a very rapid disintegration and digestion. Of this small series, although we imbedded dirty and badly mangled tissues into healthy parts of the body, in no instance did any serious infection follow, and in the one case in which the tissues did not regenerate the necrosis did not exceed that which would have occurred under other forms of treatment.

4. Transplantation of Members from One Person to Another by a Two-stage Operation.—Our experience in imbedding devitalized vascular tissue in a healthy area has suggested the feasibility of using a similar method in transplanting a finger, thumb, or larger part of the body from one person to another. The plan would be to turn back lat-

eral flaps of skin sufficiently broad to obtain an adequate vascular anastomosis, and then to imbed the part subcutaneously, as under the skin of the anterior abdominal wall of the recipient. At the same time, without completely interrupting the circulation in the transplant, a partial affixation to the stump should be made. If at the end of nine to twelve days sufficient vascular anastomosis were found, the part is to be amputated from the donor, and at once, or somewhat later, completely affixed to the freshened stump of the recipient without being removed from the anterior abdominal wall. In doing this second operation a portion of the skin-flap of the anterior abdominal wall should form a bridge between the transplant and stump, to supplement the vascular anastomosis. At the end of ten days or more, at a third operation, the vascular attachments to the stump having been proved, the grafted part and the attached overlying abdominal skin are separated, the final plastic reconstruction of the part being deferred until some weeks later, when firm union has taken place. A somewhat similar and successful transplantation of a toe to the nose has been reported from Germany. The toe was first grafted to the palm of the hand, later amputated from the foot, the hand then fastened to the face, and the toe so sutured as to form a nose. Finally, the toe was separated from the hand and a plastic operation was performed to improve the contour of the new nose. In 1893, Dr. Robert Abbe reported a request from a man who had lost his hand that there be grafted on the stump a hand taken from a convict, which it was claimed could be secured without special difficulty. As a result of this letter Doctor Abbe recorded some early experiments that he made in the anastomosis of blood-vessels by using glass tubes. Toes have been successfully grafted by a two-stage operation from the foot to the hand for the replacement of fingers, and it would seem quite feasible, with the present development of vascular surgery, aided by the method of temporary implanting the amputated part subcutaneously, to transplant an entire hand from one person to another. In visiting some of our eleemosynary institutions one is struck by the fact that there are many individuals leading a vegetative existence with good hands and good feet, but without brains to direct them. The present tendency to efficiency and scientific conservation brings up the question as to the possible wisdom of transplanting fingers, hands, or feet from those who through idiocy or other mental affliction are unable to use them, to persons with good brains who could make use of the transplanted parts could they secure them. Such a procedure might enable certain helpless dependents to make some return to the world for their subsistence, and make amends against their otherwise absolutely useless lives.

5. Restoration of Parts Apparently Gangrenous or Dead.—A finger or hand may appear to be gangrenous and yet the necrotic process may be limited largely to the external tissue. The usual plan is to

amputate and form flaps from sound tissues, completely removing the affected part. The better plan, when the hand is involved, is to carefully investigate the affected area to see if there is not a core of living tissue from which the dead tissue may be removed. By retaining every portion of living tissue and by using skin-grafting or other measures, a mutilating operation may be avoided and a much better functional result obtained. This is well shown in the following case.

Case V.—Gangrene of the finger, seen three weeks after crush in a printing press, and treatment by weak solutions of carbolic acid. Amputation, with complete removal of the finger, had been advised. Gangrenous tissue removed, and denuded phalanges covered by Thiersch skin-grafts, resulting in the loss of but the terminal phalanx.

6. Skin-grafting and Flap-transplantation.—With certain restrictions flaps of skin and subcutaneous tissue may be transferred from one part of the body to another with great success. The base of the pedicle should be sufficiently broad and so placed as to assure good nutrition, and the transplant should not be so compressed, stretched, or twisted as to interfere with its blood supply. The part to be grafted should be in a clean and healthy condition, preferably covered with healthy granulations, and the parts should be sufficiently supported to prevent undue motion. Granted these conditions, the flap, as a rule, promptly adheres, and when the pedicle is separated, from six to nine days later, all of its attached portions have an abundant blood supply acquired from the new source. Perhaps the most frequent example of such a type of transference is that to the hand. Crushing or other mutilating injuries or burns so frequently destroy large areas of the hand that extensive grafting is desirable. The Thiersch or Reverdin type of graft may be unsuited, because it is delicate and supplies only the upper layers of the epidermis. The thicker Wolfe grafts we have usually found unsuccessful, unless made very thin.

In selecting a pediculated graft the character of skin used deserves consideration. In grafting to the hand the abdominal skin is most available. It is rather thick and often has an abundance of subcutaneous fat, which should be preserved to avoid interference with the nutrient blood supply. After transference the subcutaneous fat may prove objectionable or a local obesity may follow, but this may be remedied by raising an edge of the adherent flap and carefully dissecting out sufficient fatty tissue. Where denuded tendons or open joints are to be covered, the fatty tissue is desirable, as it forms a mobile elastic layer capable of conversion into tendon sheath or synovial membrane.

The conventional type of transference of skin-flap from the abdomen to the hand is by the use of a double-pedicled vertical flap. Before placing the hand in position the flap is pulled to one side, and after a little undermining the adjacent skin-edges are united,

except at their upper and lower portions, by interrupted sutures. A gauze pad is placed between the line of union and the palm of the hand. After the flap is properly fixed by non-constricting silkworm-gut sutures a voluminous gauze dressing is applied and the hand and arm fixed to the body by a plaster cast containing reinforcing strips of metal. Three days later a window may be cut through the cast, the graft inspected, and the soiled gauze replaced by fresh material. The free use of a dusting powder composed of boracic acid and chloretone is of some value in preventing decomposition of the wound discharges. At times the projecting thumb interferes with the plan of the graft, and for certain of these cases I devised a plan by which two single-pedicled grafts are employed. The adjacent skin surfaces slide by each other, enabling an immediate closure of the abdominal defect. This method, however, suggests itself of value for only the exceptional case. If the defect be upon the palmar surface of the hand, the operations described are not available, as the hand can not well be placed so that the palmar surface will be anterior. In such a case the imbedding of the hand in a flap upon the buttock has been suggested. La Place reports that his patient found the position of the arm during the period of fixation very irksome, although the transplant was very successful. More convenient and fairly comfortable to the patient is a flap taken from the lumbar region, which we have successfully employed.

For some years, however, in grafting to the hand or forearm, we have only used skin-flaps taken from the anterior abdominal wall. Using a single-pedicled flap attached above, the transplant may conveniently be made to either the palmar or dorsal surface of the forearm or hand. From the anterior abdominal wall one can secure the largest and thickest flaps, and we have devised methods for the closure of the defect left after removal of the flap.

For the foot, ankle, or leg we obtain flaps from the opposite calf, or, if large, from the opposite thigh.

ILLUSTRATIVE CASES

Restoration of Function of Thumb After Fourteen Years.—Miss X., age eighteen years. When four years of age patient's clothing ignited from a stove and she was severely burned about the neck, lower face, body, and left hand. From the cicatricial contraction the thumb of the left hand was pulled up against the wrist, where it remained until the patient was fourteen years of age. The thumb was entirely useless, could not be moved, and the metacarpo-phalangeal joint was distorted by the abnormal position. When the patient was fourteen years of age the cicatricial tissue was divided and the thumb straightened. After this operation, from the process of cicatrization the thumb was rapidly

pulled back to the old position, and the deformity, if anything, was increased. The patient was first seen when she was about eighteen years of age. Under ether, the thumb was straightened with difficulty after dividing a large quantity of cicatricial tissue. A flap of skin with the pedicle near the wrist was raised from the dorsal surface of the hand between the first and second metacarpal bones. This was slid around in front of the thumb and was used to cover the large area formed by dividing and removing the cicatrix. To complete the closure of the denuded area and to add an opposing line of cicatricial traction, a flap was also raised from the palm and slid outward to join that taken from the back of the hand. This tended to produce tension away from the wrist. There was slight necrosis of the apex of the dorsal flap only, and no tendency for the deformity to be reproduced. Although the first joint of the thumb is the seat of fibrous ankylosis, and the outer surface of the last phalanx is somewhat flattened and deformed from the prolonged pressure against the wrist, the functional result is entirely satisfactory.

Crush and Burn of Dorsum of Hand—Articulations Opened and Infected, Bone Denuded—Successful Transplant from Abdominal Wall.—Miss X., age twenty-one, laundress. While attempting to apply a felt cover to a mangle the roller moved, pulling the patient's hand in the machine. The back of the hand, being against the hot roller for a number of minutes until the machinery could be reversed, was seriously burned, so that the finger-nails exfoliated and nearly all the joints and the posterior surfaces of the bones of the fingers were exposed. Practically all of the soft tissue on the back of the fingers was destroyed, and as pus began to form in the open joints the denuded areas of bone were trimmed off with a burr, the wound was carefully cleansed, and the hand imbedded under a vertical, double-pedicled abdominal flap, April 15, 1905. Ten days later the pedicles were separated. The patient left the hospital 19 days after admission with joint function largely preserved.

Small, horn-like thickenings at the ends of the fingers remain as remnants of the nails and the index- and little fingers. Some webbing of the fingers due to the imperfect division of the flap is present. The patient married, and considers secondary contouring operations unnecessary.

Partial Crush of Hand—Treated by Skin and Tendon Plastics. Mabel, age fifteen, mill girl. On October 29, 1906, the patient caught her left hand in the gears of a roving frame in a worsted mill, badly crushing and lacerating the little finger, and to some degree the ring finger. She was taken to the hospital, where amputation was advised, but refused. As the crushed finger healed, cicatricial tissue pulled the

little and ring finger down against the palm of the hand. An operation was done, consisting of simple division of the cicatricial tissue. This was promptly followed by recurrence of the deformity. The patient was referred by Doctor Ridpath in January, 1907. A long flap, with its base upward, was taken from the posterior ulnar surface of the hand, the palmar cicatricial tissue divided and excised, and the flap swung to the front of the hand to cover the area. There was some necrosis of the distal part of the flap, and a slight flexion of the finger persisted.

On April 7, 1907, the patient was readmitted to the Samaritan Hospital. The finger at this time could not be properly flexed, and a plastic operation, to free and lengthen the tendons and to secure more mobile skin over the palmar surfaces of the little finger, was performed. The patient remained in the hospital but one day. The patient was seen December 4, 1910, and almost perfect functional restoration found.

Crush of Hand, with Loss of Tendinous Tissue, Bony Deformity, and Ununited Fracture—Skin, Bone, and Tendon Plastics.—Charles ——, age twenty-four, machinist. On May 29, 1908, his right hand was caught between two pieces of a steel planer working at forty horsepower. The metal pieces approximated to within one-half inch. The skin of dorsum of hand was lacerated, with compound comminuted fractures of third and fourth metacarpal bones. Metacarpo-phalangeal joint of thumb opened. Extensor tendons of index-finger and ring fingers divided and lacerated. Treated by replacement of bone-fragments and suture of skin and tendons. Suppuration followed and gauze drainage was used for two months. After healing, patient could not close fingers, although there was slight flexion of terminal phalanges. The stiff joint of thumb improved under massage.

First seen September, 1908. *Operation.*—Tendons isolated from bone and skin, lengthened by splitting, united and insulated by fat. Callous thickening of metacarpals removed. Good union of soft tissues followed, but the bone did not unite. On February 14, 1910, movement had improved, and at third operation the callous was resected and an ivory peg inserted in the second ununited metacarpal. In December, 1910, the patient was found to be working daily, with good use of hand. There was no residual tenderness. There is slight deformity and fair joint movement. A residual deformity of the proximal joint of the index-finger prevents full flexion.

Deformity of Right Hand Following Severe Burn and Crushing. —*Case XIV:* Caroline P., aged fourteen. In 1912 the patient's right hand was drawn into a mangle and burned and crushed nearly to the elbow. One year later, on admission to the Samaritan Hospital, a marked contraction of the extensor muscles was found, with bony ankylosis of the second joints of the index, middle, and ring fingers, and extensive doral cicatrix.

Operation, December 8, 1913. Arthroplasties. Flaps of fat used to line joints of second and third fingers. Cicatrix excised and dorsum of hand covered by a large, single-pedicled flap from abdomen. Eight days later the flap was separated and the abdominal defect closed. Seventeen days later the transferred flap was partially contoured, and later the fat was excised and the fingers contoured.

Flap-transplants from Back and Abdomen to Correct Cicatricial Contraction of the Palm of the Hand.—Margaret, age twenty-two, laundress. In August, 1906, the patient's hand was caught in the roller of the mangle, crushing and severely burning the hand. The patient was under the care of a physician for about six months before healing occurred. As a result of the contraction of the large palmar scar the fingers and thumb were so pulled together as to render the hand nearly useless. The patient entered the Samaritan Hospital, June 7, 1917. Under narcotic anesthesia the cicatricial tissue was dissected from the palm of the hand and two vertical incisions made over the left loin, the skin raised, and the hand passed behind the back and slipped under the flap. The pedicles of the flap were divided on the tenth day and the patient discharged on the thirteenth day. The grafting was successful.

The patient was readmitted to the Samaritan Hospital, October 2, 1907, and the portion of flap which formed bridges between the fingers, divided, and by the aid of plastic displacement of the adjacent skin the condition of the hand improved. The patient was discharged on the thirteenth day.

The patient was again admitted to the Samaritan Hospital, November 1, 1908. The lumbar flap was not of sufficient size to permit complete extension of the fingers, and especially did not give sufficient tissue between the thumb and index finger. A single-pedicled abdominal flap was then raised from the upper left abdominal quadrant, the cicatricial tissue removed, and the flap, with its base uppermost, accurately sutured over the palm of the hand just above the previous dorsal flap. The patient sat up on a back-rest on the second day, was out of bed on the third day, and the graft was separated and by further plastic procedure arranged in position on the eleventh day. Five days later the patient was discharged from the hospital. After this operation the patient was able to use the fingers and thumb fairly well, and continued her work as laundress for over a year. A progressive deposit of fat under the abdominal flap formed an undesirable pillow-like protrusion, and for this the patient was readmitted to the Samaritan Hospital in November, 1910, the edge of the flap raised, and the excess of fat removed. At the same time further plastic procedures were undertaken to reduce the webbing of the fingers. No necrosis or infection occurred

in the flap after any of these procedures. All the fingers and the thumb can be freely moved, except the intermediate joints of the index-finger.

Volkmann's Contraction of Hand and Forearm Following Prolonged Use of Splints—Flap-transplantation from Abdomen, with Improvement.—John ——. Fracture of left arm in 1909 treated by application of anterior and posterior splints for almost one year. Ulceration and Volkmann's contraction, with loss of skin, muscles, and tendons on anterior surface of forearm. Operation on back of wrist with slight result. First seen January, 1910. February 13, 1910—Transplantation of quadrilateral flap to forearm and hand, after removal of much cicatricial tissue. Marked improvement.

Crush of Foot Under Car—Restoration of Weight-bearing Sole from Opposite Calf.—William ——, age twenty-five, brakeman. On August 2, 1907, while standing on a box-car, was struck by a bridge and fell to the ground, striking on his head and right shoulder. The wheel of the last truck passed over his right foot, crushing the bones and lacerating almost the entire dorsum, crushing off the greater part of the sole back of the ball of the great toe. The lacerations extended on to the dorsum of the great toe, two inches above the internal malleolus, and on the outer side to the lower border and anterior surface of the external malleolus. After four or five weeks much of the dead tissue had been cut away and Thiersch's grafts from the thigh of the same leg were applied under spinal anesthesia. These grafts united successfully, but in February, 1908, as the lower part of the os calcis formed a keel-like ridge over which the skin was continuously ulcerated, the ragged bone was removed, the area denuded, and a pediculated flap covering the heel and half sole applied by partially imbedding the foot under the skin of the calf of the opposite leg. One week later the pedicle of the flap was divided and the foot separated, the denuded area of the calf being covered by Thiersch grafts. One year after injury the patient could walk without crutches, and two months later he resumed his occupation. The patient can flex and extend all his toes. There is no inconvenience from the opposite calf.

Deformity of Foot from Deep Burns and Cicatricial Contraction. Flap Transplantations from Opposite Leg.—*Case XIII:* William R., aged twenty-six. When ten years old patient stepped in hot cinders, deeply burning the right foot and leg. The toes were almost entirely destroyed, and ten years were required for healing. When twenty-four years of age the foot was again burned, and the dense cicatrix refused to heal. Two years later (September, 1912) the patient was admitted to the Samaritan Hospital, the large, ulcerated scar partially excised, and the foot successfully imbedded under a flap taken from the left calf. At this time additional grafting by Wolf's method

failed. A later attempt with Thiersch grafts having failed, seven months later a successful flap transplantation from the left thigh to the outer side of the heel was done.

Six months later, it having been found that a small ulcer on the foot was a Marjolin's ulcer, and that there was carcinomatous metastasis in the pelvis, an interilio-abdominal amputation was performed. The patient resumed work, but later developed other metastasis and died.

INSTRUMENTS OF PRECISION FOR THE PERCY TREATMENT OF UTERINE AND OTHER CANCER

A. The Electropyrometric Heater
B. The Distensible Hydrothermotaxic Heater

BY A. ERNEST GALLANT, M.D.
AND
L. HOWARD MOSS, M.D.,
NEW YORK;
PROF. LOUIS BLISS AND E. N. LIGHTFOOT,
WASHINGTON, D. C. NEW YORK.

The purpose of this communication is to present for your inspection and consideration two newly designed instruments for the accurate application of a low degree of heat (Percy's method) for the devitalization and destruction of cancer involving the uterus and vagina, the alimentary tract and other cavities.

It is to J. C. Percy[1] of Galesburg, Ill., that we owe a debt, as the first to apply, in a curative way, the well established principle that the continuous application of a relatively low degree of heat, 43° to 46° C., when delivered directly into the cancer mass, for from 20 to 60 minutes, will cause a disintegration and destruction of the malignant tissues to a depth of from two to three or more inches outside the point where the heat is applied, and that without injury to any of the contiguous healthy structures.

In thus applying heat Percy made use of an electrically heated plumber's soldering iron, the copper heads being modified in shape to resemble the tips of a Paquelin cautery.

When we take into consideration the facts that most of Percy's patient's were "of the utterly inoperable cases, the kind with 100 per cent. mortality,"[2] with some alive after two, three, four, and even seven years, we must admit that the method has a definite place in the treatment of uterine and vaginal cancer. In brief, Percy's technique is: (1) Open the abdomen. (2) Use a low degree of heat. (3) Pass the heating head through the cervix to the fundus; keep it in one position until the whole mass contiguous to the heating iron is made so hot that it cannot be held longer in the surgeon's hand when incased in a medium weight rubber glove. (4) Apply the heat until all the structures that were fixed at the beginning of the application are freely movable.

After witnessing Percy demonstrate his method at the General Memorial Hospital, and listening to his paper[3] before the Academy of Medicine, New York, April 15, 1915, and a careful consideration of

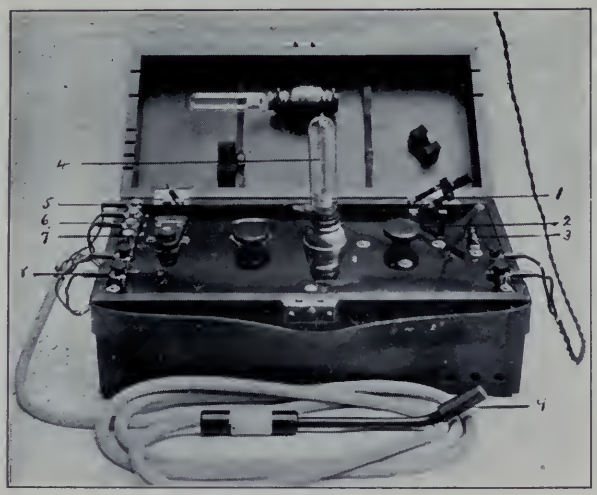

Fig. 1.—Electropyrometric heater: 1, heating switch; 2, rheostat; 3, fuse; 4, resistance lamp; 5, test switch; 6, galvanometer "tell-tale"; 7, temperature setting handle and scale; 8, galvanometer button; 9, copper heating head.

his technique, one could not but be impressed by (a) the absolute sincerity of the operator; and (b) the possibility of rendering the immobile uterus freely movable, and that without any apparent depressing effect on the patients at the close of about an hour's application in each case.

After some months of study and fruitless efforts, my associate, Dr. L. Howard Moss, was successful in interesting, from a humanitarian standpoint, the generous services of Professor Louis Bliss, of Washington, D. C., who, from our crude drawings, developed the pyrometric heater herewith shown you, and formerly presented[4] to the Medical Association of the Greater City of New York, June 15, 1916, which has been named the "Electro pyrometric heater," and offers the following special features (Fig. 1):

1. For heat localization a specially designed heating coil placed in the ½ x 2-inch copper head wherein all the heat is generated and localized within the cancer mass, the handle remaining cool.

2. Introduction through an ordinary bivalve speculum has been made easy, as the head has been united with the handle at an angle similar to that of an uterine sound.

3. Heat measurement has been accomplished by inserting in the head the wires of a thermocouple that registers the actual degree of

heat generated in the head, which can be adjusted to any temperature between 100° and 200° F.

4. Heat control is obtained by "setting" the regulator at the desired temperature, turning the rheostat and pressure on the "tell-tale" which will indicate if the heat being delivered in the head is above or below the desired degree.

5. Heat safety is insured by a very delicate fuse protecting the patient and instrument from short circuiting.

6. Heat dissemination can be facilitated in the enlarging cavity, as the treatment progresses, by slipping over the head metal caps ¾ and 1 inch in diameter.

7. Heat radiation—From our limited experience in one human patient, and numerous experiments with animal and vegetable tissues, we find that owing to the rapid distribution of heat from the considerable area of the surface of the head, there is a difference between the internal and external temperatures of from 15° to 20° F.

The following is the report of a case of inoperable epithelioma of the cervix, uterus and broad ligaments, treated by the pyrometric heater:

Mrs. C——, aged 47, multipara, last menses four years ago. For the last nine months has had a bloody vaginal discharge, with a very bad odor; alternating constipation and diarrhea; dysuria. "The pain is wearing her out." She had made arrangements to enter a home for incurables, but learning of the "heat" treatment, entered the service of Dr. N. C. Goodwin, at the Jamaica Hospital, who made a cystoscopic examination and found disseminated ulceration of the vesical base. Examination showed that the cervix had been removed, leaving an inverted cone leading into the uterine cavity, but 2 inches to the fundus, and the whole firmly fixed by the thickened broad ligaments out to the pelvic walls.

Jan. 3, 1917.—The first "heating" lasted an hour, with the galvanometer "set" at 138 F., and the heat developed in the uterus at 106° to 108° F. One hour prior to the treatment a hypodermic injection of morphine, gr. ¼, hyoscine, gr. 1/100, and cactin, gr. 1/67. At first she was a little nervous, but dozed from time to time, occasionally complaining of backache, which she attributed to the lithotomy position. The application was made through an ordinary Graves' bivalve speculum. During the following week she lost considerable blood, but the vaginal odor was much less evident. Jan. 17.—The vault presented a craterlike appearance. The heating lasted one hour, at the same temperature as before, and during the next three weeks the bleeding stopped, the odor was no longer obnoxious, pain lessened, the appetite and sleep were markedly improved, and she sat up almost daily. No morphine was given for pain after the first treatment, but she was very homesick for her children. Feb. 3.—The excavation has nearly doubled in size, the edges of the vaginal vault came together when the speculum was removed, and we felt greatly encouraged at what was being accomplished. The third heating of one hour was given, but a few days later her friends (?) took her from the hospital to the home for incurables, though it was evident to all who saw her that she was improving in every way. We have no opportunity to follow up the case.

However, we had learned (a) that a temperature as low as 108° F.

would and did devitalize cancer tissue; (b) that it would stop hemorrhage and odor, and lessen pain; (c) that it was followed by absorption and temperature; (d) that the patient's condition improved in every respect; and (e) that with the pyrometric heater the heating could be made without anesthesia, through a bivalve speculum, without opening the abdomen; and last, but not least, that though our instrument was built to develop 140° F. in the heating head, it would have to be changed to attain a much higher temperature; and that only experi-

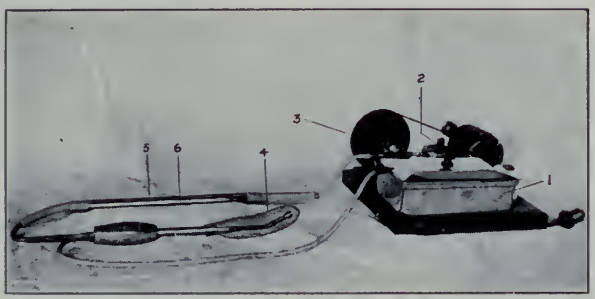

FIG. 2.—The distensible hydrothermotaxic heater: 1, water pan; 2, heat regulating switch; 3, motor driven pump; 4, double current applicator enclosed in a rubber bag; 5, glass tube, enclosing thermometer 6.

ence can demonstrate just what the temperature will have to be to deliver 120° F. (or higher) into the tissues, the degree which Percy seems to imply is necessary to penetrate deeply into the tissues, and destroy the whole of the pelvic neoplasm.

We can but feel that with the right degree of heat, applied through the pyrometric heater, the local destruction of cancer can be effected.

While the pyrometric heater was in course of construction, I became obsessed with the idea that the use of hot water as a heat conductor might afford several advantages, and, through the untiring efforts of Mr. E. N. Lightfoot, herewith we present, for the first time, the result of the past two years' work, which has been christened (Fig. 2) "The distensible hydrothermotaxic heater," the components of which are:

A water heating system consisting of a pan (1) holding about a quart of water, under which are fastened electric elements for heating the water; and (2) a heat regulating switch which controls the current and the temperature of the water.

A pumping or circulating system—The heated water from the pan is forced by a motor-driven pump (3) through tubing and the double-current applicator handle, filling and distending the rubber bag (4) and returning through the handle, follows the tubing back to the water pan. The pumping and heating are accomplished by the same 110 to 120-volt, direct or alternating street current.

The heat regulation can be accomplished (a) by increasing the electric current to the water pan; (b) by speeding up the pump and accelerating the flow of water through the applicator, or (c) by combining these two methods.

Heat Determination—Borrowing the ingenious idea from J. J. Tate[5] a glass tube (5) inclosing a thermometer (6) has been connected up with the tubing before the water enters the handle of the applicator, and as it surrounds the thermometer in the glass tube, it permits the operator to see the exact temperature of the water as it enters (or leaves) the applicator.

For determining the degree of heat being delivered to the tissues a curved thermometer is placed between the tissues and the bag within the mass, and the reading will show the heat being delivered to the tissues at the point of contact.

Advantages of the water distended applicator for the application of water-borne heat in the treatment of cancer—The novel and most important feature of this apparatus is the dissemination of water-borne heat, through a distensible rubber bag, a method which we believe offers the following practical advantages:

1. Insertion—With the rubber bag collapsed the applicator can be easily introduced into a moderately dilated cervical canal, or through a stricture of the esophagus, pylorus, or any other portion of the alimentary canal (after opening the gut).

2. Adaptability—Under the internal pressure of the pump-driven water the bag will distend and adjust its size and shape to every nook and corner of any canal, cavity or excavation.

3. Dissemination—As water is the best heat conductor, and the thin-walled rubber bag in actual contact with the tissues, we have the most favorable conditions for the uniform dissemination and the deepest penetration of the necessary degree of heat, throughout the widest possible area, and for securing the greatest disintegration and destruction of the malignant structures.

4. The technique is of the simplest, requiring only a bivalve or Ferguson speculum; the introduction of the collapsed applicator; the raising of the water to the required temperature; the adjustment of the pumping to the necessary speed; and to keep it going for 30 or more minutes, or until the rigid mass has become mobile.

5. Drainage must be efficient to avoid absorption and can best be secured by inserting one of our two or three-inch fenestrated rubber drains, with a roll wick,[6] the latter to be changed from day to day.

6. Subsequent treatments can at any time be carried out, and as frequently as the condition seems to indicate; as the whole procedure can be accomplished without anesthesia; without opening the abdomen; without pain or discomfort to the patient, simply by the injection of

morphine, one-quarter grain; hyoscine hydrobromide, 1/100 grain, cactin, con. 1/67 grain, one hour before operation, and repeated if necessary.

Favorable reports have been made by Clark[7], Gelpi[8], and Balfour[9], who says: "Percy has developed a method which derives the full value of this agent (low heat) in the treatment of cancer of the cervix. I became interested in this method about two years ago and from experience in more than 100 cases am convinced of its great value. . . . The method undoubtedly offers more to the patient with advanced cancer of the cervix than any treatment with which I am familiar. Its value is so definite in the advanced stages that serious consideration must be given its possibilities in the earlier stages of the disease." If we accept these reports, then with the pyrometric heater and the hydrothermotaxic applicator, or both, we certainly ought to be enabled to avoid the not-unlooked-for results reported by Boldt[10], and Leonard and Dayton[11], where the pathological reports seem to point unmistakably to the need of just these instruments of precision which we now offer you.

From the experience of Fulton[12] with heated bougies for gonorrhea; the use of hot water in urethral stricture, by Stern[13], and our own experience[14] with a double current pelvic cooler in pelvic peritonitis, proctitis, etc., it would seem that the field of usefulness for the distensible hydrothermotaxic heater may be a widely useful one.

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DISCUSSION.

Dr. Robert T. Morris said that in the hands of an expert like Dr. Gallant the Percy treatment for uterine cancer might give results that were worth while in selected cases. There have been too many reports of sloughing and of sepsis following the Percy treatment to allow of surgeons showing much enthusiasm over the new procedure. We must always remember that we are not applying a curative method anyway, but only a palliative resource that would lessen the discomfort of some

patients to a marked degree. We must be on guard about the overstatement of benefit which cancer patients are prone to give. There is a peculiar cancer psychology. Patients with almost any form of malignant disease are eager for operation, and they magnify any sort of improvement in a way which is apt to be misleading. That will explain the success of cancer charlatans who secure a large following, and who readily obtain large amounts of money from patients who can ill afford to pay for services which eventually will prove futile in so far as cure is concerned.

PROGRESS IN SURGICAL THERAPEUSIS

BY ALBERT VANDERVEER, M.D.,

ALBANY, N. Y.

The title of my paper gives great latitude regarding the extent to which the subject may be approached. Taking advantage of this, I shall refer to but a few of the points upon which I can speak from personal observation and experience.

There is much in the surgical therapeutics of to-day that seems thoroughly reliable for us and beneficial to our patients, and yet it is too true that comparisons can be made relating to certain forms of sepsis, in which results are not much better than four decades ago. Laboratory research has done much to aid us in our precision of diagnosis, but on the other hand have we made that progress in treatment consistent with these advances? If we are candid with ourselves, must we not admit that there are too many deaths from septicemia, not only among members of our own profession, but among patients from all the various walks in life; not in one city or section, but from our country at large? To express my convictions that in our studies regarding laboratory experiments and results I am convinced that we have placed too much confidence in the mildness of certain forms of pathogenetic microbes, and forgotten somewhat our long-established knowledge of the histology and location of certain anatomical structures. We must harmonize our knowledge and become more alert in the application of wisdom.

A man at my time of life may be presuming in asserting that there are many divisions of bacteria, and various microscopical organisms that are not fully understood in their seriousness, when aroused into action, especially in structures possessing little resistance, and in alarming proximity to important organs. We are only beginning to understand that there is a variety of staphylococcus aureus much more virulent than we had ever supposed, and this observation applies to other more precise classification and new discoveries. We also understand that there are in one organ latent pathological organisms that may be started into activity by an operation, and, having an affinity for some important organ elsewhere, do serious damage. Witness what we are only beginning to recognize, and not fully understand, of myocarditis and acute dilatation of the heart in connection with our gall-bladder work.

Case I.—Mr. W. L., æt. 47, a man of excellent habits, very active in business. For nearly two years he suffered more or less from acne vulgaris, located, more

especially, over upper part of back and in region of neck, assuming a condition of true furunculosis. Cultures developed the staphylococcus aureus, and under the use of autogenous vaccines he improved decidedly for a period of six months or more; then a return of the trouble presented itself. He was examined with the utmost care by his physician, who had treated him for a long time, and an *x*-ray of his teeth showed that the root of a molar in the upper jaw—the tooth having been crowned for nearly two years—presented evidence of infection. The crown was removed, a few drops of pus escaped, and after this the patient made a somewhat rapid recovery. The tooth was treated and left open for a long period. The patient spoke most decidedly of the improvement in his general condition after this treatment, and he is greatly impressed with the belief that many of his former symptoms of exhaustion, and, at times, inability for prolonged exertion in his business, were due to this septic tooth. In a fairly short period his boils disappeared and there was no recurrence.

This and other cases are not presented as perhaps demonstrating a fixed principle to guide us in the study of our pathology, but as having some bearing upon our therapeutical investigations. It matters not what may be our treatment for the relief of pathological lesions, since it is becoming more and more demonstrated that bacteriological examinations of secretions and discharges, and the researches constantly going on in our laboratories, are becoming of great value, and that such thorough investigation of surgical lesions is indispensable. It reverts to the principle that settled in upon my convictions of many years, that when our patients are not recovering along such lines of treatment as we had expected in confirmation of our diagnosis, time passing, we cannot be too energetic in reviewing the situation, in going over the patient's history and symptoms. Every possible condition, such as boils, tonsils, septic teeth, various sinuses, results of old surgical lesions, or of physical ailments that may have prevailed at one time, should be investigated with the utmost care, and we must include a thorough laboratory study of the secretions from the auditory canal as well as the nose and the Eustachian tubes. In fact, no part of the human body should be slighted ere we call a consultation.

The keen, up-to-date consultant will have all the more confidence and respect for the practitioner of medicine who covers the ground so thoroughly. It may make his study of the case exceedingly difficult. He will consider himself very fortunate, when he is called in consultation with such an exact practitioner; therefore, although no hidden factor in the case be found, the consultant with a broad view of the situation will not infrequently coincide with the diagnosis, and then be able to mark out a line of treatment somewhat different; in this manner he adds much to the therapeutical atmosphere of the situation.

Our laboratory researches of to-day place us upon a more solid foundation with reference to the proper understanding of the examination of the blood, the urine, the secretions that come from mucous surfaces, and as the result of laboratory research we can readily understand certain

symptoms along lines of absolute knowledge, especially in regard to the mouth. Perhaps at no time has there been a greater interest than at present in reliance upon the importance of making a correct diagnosis regarding infection of joints, in the disturbance of certain functions pertaining to the muscles or nerve centers, in going over more thoroughly a tonsil that in the past has not attracted very much attention. A more careful observation of conditions may assist materially in determining a line of treatment that will lead to recovery of the patient.

Case II.—Somewhat recently I had my attention called to a patient, a lady, æt 60, with a previous history of excellent health, who had every possible comfort, but who, for a period of two years, had suffered from supposed rheumatic conditions with, at times, a painful condition of the neck resembling incipient torticollis, with that marked lameness of the knees that led to the diagnosis of a supposed broken arch. She wore most persistently a metal support, but with no permanent improvement. Her teeth had had admirable treatment by a very competent dentist. Since she did not improve, it was suggested that a warmer climate might be beneficial. As she was leaving, her dentist advised an *x*-ray of her teeth, but this was not possible at the time. The months of change of climate did little good, so she was finally persuaded to make an extra trip in order to consult a very competent radiographer. However, before doing this, it was thought advisable for her to consult a nearby, exceedingly good dentist, for examination of what was called a double crown of the two molars in the upper jaw, the work having been done two years previously. At that time it was stated that the one tooth was not free from an ulcerative process of the root, but the root had been carefully filled, and a crown surrounding this tooth, together with the one fitted over the next tooth, which was supposed to be free from any disease, was removed. This double crown formed a bridge holding the diseased tooth more firmly, but when the dentist separated the bridge and took out the tooth that had been filled, it was found to be in a most marked condition of advanced caries; in fact, the root that had been removed was immediately recognized as the source of the secretion that had been escaping into the patient's mouth for a period of eight or ten months. At the time she thought it came from an abscess connected with the tooth, but of these conditions patients are often not so concerned as they should be.

After this treatment she had an explosion of symptoms. Her neck was much worse, and she had an acute exacerbation of pains about the knee joint, all of which improved later. But the condition of the muscles of the neck did not progress, as it was hoped. The *x*-ray examination showed that the cavity of the tooth had healed and that the adjoining tooth was in good condition. But the *x*-ray picture of the neck showed a decided spur projecting from the fifth cervical vertebra—not the development of an extra rib, but a condition that probably had had much to do with her disturbed lesions. The patient has improved, while taking treatment at one of the sulphur springs of the Middle South, increased comfort coming to her, her friends, and her physician, in knowing that a more correct diagnosis had probably been reached.

Case III.—An excellent physician of middle age, in the enjoyment of a well-earned practice, had felt, for a period of two years, a reluctance to and difficulty in doing his work, but no observations of his own nor examinations made by competent associates seemed to reach a positive diagnosis, whereby treatment granted any relief. Finally, the suggestion was made that he have his teeth examined, due, somewhat, to the fact that he had had considerable work done on them for a period of two or three

years. This *x*-ray examination demonstrated that a crowned tooth had a well-marked lesion about the root. The crown was removed and the tooth treated partially. It was not filled, but an attempt was made to keep it in an aseptic condition, and in six months he was so decidedly improved that it was fair to assume the cause and effect, in that this tooth was undoubtedly septic and the absorption gave him much of the uncomfortable distress from which he had suffered."

I should say that in the former case a very careful blood examination had been made, the patient stating that nothing was found to aid in a better understanding of her case. In the latter case it was said that the result of the examination showed profound anemia.

I am speaking of these cases, not arranging them on the basis of a scientific paper, but perhaps to demonstrate that there are yet conditions where much good can be derived from a more thorough effort at diagnosis, and which, from the surgical side of our practice, really becomes a therapeutic agent.

Lesions of the joints, lesions of the muscles and of the nerves, of the various sinuses, and other regions of the body, not responding to prolonged medical treatment, eventually drift into the hands of the surgeon, or a consulting surgeon, and whenever operative intervention can be avoided and therapeutic remedies made use of it is certainly much to our credit to take advantage in that direction.

To every surgeon the secretions of the mouth have been a source of anxiety for years. One who has been in practice for any length of time will call to mind a not infrequent number of serious lesions that have resulted from puncture about the edge of the finger nail, from the bristles of a nail brush, when a rapid infection occurred, and abscesses developed along the forearm and in the axilla, requiring decided surgical operative intervention. In many of these cases the recovery was somewhat tedious, and there was a mortality list.

The surgeon of much experience will look upon these conditions with as much apprehension as he looks upon the cases of the abscess or furuncle that appears about the angle of the nostril, about the lip, or within the nasal outlet. We know how exceedingly dangerous they may be.

In the Mayo Clinics, Vol. 6, Charles H. Mayo has published a valuable paper on "Mouth Infection," referring more especially to pyorrhea and like conditions, but it requires a much more extensive study on the part of the members of our profession to grasp its full meaning. He refers to Rosenow's great work, with an indorsement resulting from a very large experience, and I make the following quotation, as it seems to be so very appropriate here: "The physicians engaged in this line of observation require fully as much training in the rudiments of dentistry as the dentist does in the signs of infectious diseases. While we have leaders in all professions, through the energy

of their kinetic glands, the 'big stick' which leads to our advancement is in the hands of the progressive and educated public, who are constantly demanding more of their dentists, of the medical profession, and of the State in protecting them against preventable diseases.

In days past, when our bacteriological examinations came to us, we felt somewhat comforted when the report of *staphylococcus aureus* was obtained, realizing that the condition was not so serious as the case presenting streptococci. Now, recent laboratory investigations and the reporting of a fatality that has continued, teach us that this form of staphylococcus has a virulency that must be respected, and reached promptly when once the symptoms and examination tell us of the danger. To-day the bacteriological work is giving the surgeon the greatest help that has been presented at any time since our understanding of cultures, as well as the classification of bacilli, and association of micro-organisms. Therefore, I want to emphasize that we must encourage efforts in investigation, that therapeutical agencies must be recognized and employed to bring as favorable results as do the most difficult operations, or exhibiting our surgical skill to the utmost. As professionals we are far from being perfect in our diagnosis. Amidst all our wonderful progress in surgical work our laboratory autopsies show an unmistakable record of errors. Let us, therefore, be reasonable and sensible with one another, and, wherever possible, gain a point that will enable us to become clearer.

I think that when a surgeon has reached my time in life, and has passed through decades when nothing was known of bacteriology and laboratory research, he may, with the profoundest gratitude, refer to the advances that have come to that branch of his profession due to the pathological studies and investigations of the laboratory. And I now wish to emphasize that no surgeon can be successful without encouraging and employing to the fullest extent the aids rendered by the splendid workshops that are now in all our medical centers.

When we consider the great advances made in the last decade in the study and understanding of pathogenetic micro-organisms, there are too many fatalities, especially among the members of our own profession. In our midst death stalks, and we apparently are left helpless in the cases of septicemia that baffle our every effort.

THE MENACE OF MOUTH INFECTIONS

OLIVER T. OSBORNE, M.D.,

Professor of Therapeutics, Yale University School of Medicine,
NEW HAVEN, CONN.

There is no more impressive sequence than the presence in a patient of a disease or abnormal condition, such as infected teeth or gums, and the later surgical eradication of the focus of infection; or, to make the sequence terse and logical, let us put it thus: patient; ailment: crowned, bridged or decayed teeth, inflamed gums, or pyorrhea, or all of these things; roentgenograms of these suspected areas demonstrating pus and degenerated bone; operative demonstration of pus sinuses and cheesy, broken-down bone; and lastly, but unfortunately not always, the cure of the patient.

In this age, in which the laity has acquired from periodicals a smattering of medical science, and therefore thinks it has a perfect right to criticize medical men and to ridicule what they term "medical fads," let me urge that the nearest relative of the patient be present at the dental operation, and be placed in close proximity to the foul tooth, foul crown, or foul pus that is extracted from the mouth of the loved one. I know of no more impressive demonstration to the ordinary layman, and he often becomes a hysterical enthusiast for the removal of infected teeth, or even of those that may possibly be infected.

MENACE OF CROWNED TEETH

Cruelly awakening to the physician is the demonstration of a bacterium in the blood or in a distant lesion, and a late demonstration of the same germ in an extracted tooth or in the secretions of a pocket in the gum. I do not believe that there is a greater menace to health today than crowned and bridged teeth, to say nothing of imperfectly filled and dead teeth, and of pyorrhea alveolaris. Furthermore, infection of the tonsils and the sinuses adjacent to the nose must never be overlooked. If such infection has not caused symptoms, it will do so, and its eradication is the only safety.

From infected areas in the mouth many pathogenic organisms have been isolated, probably the most dangerous being the *Pneumococcus* and the *Streptococcus viridans*. We do not know how many pneumonias, following or accompanying influenzal affections, occur, because pneumococci are being carried in the mouth. We do not know how

many times irregularity, weakness and actual disease of the heart are due to germs harbored in the mouth. Neither do we know how frequently the *Streptococcus viridans* is the cause of heart disease or adds its fatal potency to an already established chronic disease.

We do not know much about the *Entamoeba buccalis,* but we do know that it is probably always accompanied by other germs, and especially by the pyogenic germs. Pyorrhea alveolaris is unquestionably due to infection, but this kind of infection and inflammation does not often occur unless there is degeneration of the gum tissues, and such degeneration most frequently occurs after 40 years of age. It may be here noted, parenthetically, that chronic colitis, or at least decomposition in the colon, also occurs most frequently after the age of 40, and both of these conditions are very frequent in people in middle life. Is the intestinal disturbance a sequence of the mouth infection?

Connellan and King[1] have isolated a non-pus-forming diplococcus which they believe produces dangerous toxins. They find these germs in the crypts of tonsils, and patients suffering from arthritis, asthma, endocarditis, myocarditis or nephritis have been found to harbor these germs in their mouths. They advise producing an autogenous vaccine and using this for some time before such diseased tonsils are eradicated.

It is not my purpose either to offer or to discuss roentgenograms of damaged teeth and gums; but let me assert that no dentist should devitalize, or attempt to fill the roots of a devitalized tooth, which is to be preserved, without the aid of roentgenograms; that every case of pyorrhea alveolaris, every suspicious root, and occasionally all crowned and bridged teeth should be subjected to the scrutiny offered by the roentgen ray. It is useless to agree on the removal of one infected tooth and possibly leave other infected teeth in the mouth of the patient, and yet such carelessness is repeatedly agreed to by both physician and dentist. Also, it is difficult to compel a dentist to operate immediately on all infected areas. He does one thing at a time, and then takes up something else. What surgeon would remove one point of infection and leave half a dozen others, or even one other infected area?

There must be hearty medical cooperation between the physician and the dentist in order to decide, in any individual patient, what teeth shall be preserved, what teeth must be removed, and how best to treat infected gums; also what part a diseased condition of the patient plays in the mouth condition.

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[1] King, J. J.: Further Observations on the Connellan-King Diplococcus Throat Infections, *The Journal* A.M.A., Jan. 13, 1917, p. 91.

M. I. Schamberg[2], a noted New York dental surgeon, says:

> Crown and bridge work, as well as all work upon pulpless teeth, should be conducted by men who would specialize in that work, and who would, through the medium of x-ray, satisfy themselves that they are not putting a beautiful super-structure on a weak foundation. Roentgenograms should be taken from time to time after the insertion of such pieces, to determine the state of health or disease of the hidden parts. Patients' mouths should be kept free from infection at all costs, even though it should mean the removal of every tooth in the head. If it can be done without sacrifice of the teeth, so much the better, but a toothless mouth is to be preferred to one containing a single focus that menaces the health of the patient.

It should also be urged that however well a patient is, these germs of infection, wherever they may be, are ready to do him some injury whenever an acute infection attacks him, or when his own systemic strength is in any way reduced. They are all waiting an opportunity, and how can we excuse a physician for omitting to study his patient's mouth? How can we excuse the dentist who waits until to-morrow, or next month, or six months hence before he removes a source of infection which he has recognized? Or how can we excuse a dentist for carelessly constructing bridges or crowns in the mouth of a young patient, knowing the danger from infection in the years to come? In other words, have we the right to crown to the gums, even if they are wonderfully well fitted? Have we the right to construct permanent bridges, when an aseptic bridge or a removable plate is more sanitary?

IODIN INJURIOUS

I do not propose to discuss the treatment of pyorrhea alveolaris, but let me emphasize the fact that dentists use iodin too freely on the gums. A little pain here, or a little infection there, and the gum is injured by repeated applications of iodin. We know the value of iodin as a counterirritant or as a germ destroyer. We also know that it destroys the vitality of tissues, and many a gum has been burned and blistered, and inexcusably made a region for more infection. We should remember that there are always germs in the mouth, many of them harmless, but also many ready to attack a broken mucous membrane or ready to be absorbed into the system through such a lesion. Therefore, care should be exercised not to injure the mucous membrane of the mouth or gums, especially when an infection is being treated.

I find that infected teeth and tonsils are frequent causes of thyroid disturbance, causing both hypersecretion and hyposecretion, and no medicinal treatment will effect a cure until the foci or infection have been removed. The absorbed toxins produced by the germs of infection and by the local suppuration often act peculiarly on the thyroid gland. The thyroid may be considerably enlarged, yet may give abso-

[2] Schamberg, M. I.: Journal of the Allied Dental Societies, December, 1915.

lutely no symptoms of increased secretion and need not be cystic. Something irritates the gland, and then something else inhibits the result of its increased activity. This is shown by the surgical removal of the source of the mouth infection, and sometimes marked symptoms of hypersecretion immediately occur. I have seen three such instances. In one case the gland became greatly enlarged after the operation, exophthalmos occurred, and a tachycardia of from 140 to 160 developed. Before the operation, absolutely no thyroid symptoms were present, except a slightly enlarged gland.

Not only the thyroid, but many other internal secreting glands of the body, are disturbed by the absorption of germs or toxins from the mouth. The suprarenals are, probably, especially acted on, as we have great changes in blood pressure in these patients. Many a patient with a very high blood pressure shows no arterial and no kidney excuse, no intestinal toxemic excuse, and this high pressure persists, even when the diet is made rigidly vegetarian. Consequently, it is self-evident that there is internal secretion disturbance. Whether the suprarenals hypersecrete, or the thyroid, and one or two other glands perhaps under-secrete, it is difficult to determine, but that these glands are disturbed there is no question. Also there are many instances of very low blood pressure in these patients, and again we may not know whether the toxins depress the nervous system, or the vasomotor center; or whether they stimulate the thyroid to increased secretion of vasodilator substance, or inhibit the suprarenals as to their vasopressor substance.

Not infrequently patients with glycosuria have mouth infection. These cases are likely to be without typical diabetic symptoms, namely, without polyuria, and without thirst. In these cases there may be pituitary disturbance, or suprarenal disturbance, or pancreatic disturbance, or the glycosuria may be caused by the absorption of something that interferes with the liver or with muscle metabolism.

We must recognize that germs may be present in and around gums, allowing dangerous absorption of their toxins, without any local manifestations of pus. This is true of some germs that cause arthritis.

Again, there can be no question that the constant absorption of irritants or poisons from the mouth can cause irritation of the kidneys and subsequent chronic nephritis, even if focal infection of the kidneys is not thus caused, and many a case of autogenous infection or purulent infection of the kidney occurs without any apparent tangible excuse. Probably these obscure cases occur mostly from concealed infections of the mouth, tonsils or one of the sinuses adjacent to the nose.

We do not know that this continued absorption of concealed irritants in the mouth for months and years may not cause arteriosclerosis. All sorts of gastrointestinal disturbances, such as hyperacidity and ulcer of the stomach, can be caused by such mouth infections. And let us re-

member that cancer of the stomach seems to be on the increase. Recently I saw in consultation a patient who made a profound impression on me. He was a man but little over 40, who had, before it was discovered, far advanced, inoperable cancer of the stomach, and besides several bridges, there was hardly a tooth in his mouth that was not crowned. He had been fussing with his teeth and visiting dentists for fifteen years or more.

Statistics prove that cardiovascular-renal disease is increasing enormously, and we know that, in the last twenty-five years crowns, bridges and pivoted teeth have also increased in a most extraordinary fashion. One has only to look into the mouth of every patient who enters one's office, of every patient who enters the hospital or the dispensary, to see how hard the dentists are working.

One of the saddest things that can happen to a person is infection of the blood with the *Streptococcus viridans*. This germ probably always gains an entrance through the mouth, and if we should cultivate the pus and secretions from the patients who have diseased mouths, we should probably be astonished to find the number of times the *Streptococcus viridans* was present. In the vast majority of cases the only hope for the patient with *Streptococcus viridans* is to eradicate it from the mouth before it infects his blood and causes malignant endocarditis.

The relation of mouth germs to arthritis deformans seems proved, hence eradication of the source of infection before the joints are affected should be the preventive treatment of to-day. To allow infection in the mouth to persist until this painful and crippling disease develops is inexcusable.

For nearly two years now, at a public tuberculosis institution of which I am chairman of the medical board, we have examined the mouths, corrected the teeth and removed sources of infection of every patient who entered the institution, and owing to this preventive treatment we have had less tonsillitis, fewer sore throats, less indigestion, and less influenza and colds than we had before we began these mouth investigations.

I think that both dentists and physicians have been very slow in discovering the harm done to patients by crowns and bridges, by leaving infected teeth in place, and by improperly filled teeth. Physicians do not pay proper attention to, and many times do not even look into, the mouths of their patients. I look back with chagrin and shame as I think of the probable cause of the chronic invalidism of some of my patients of years ago. But with this admission of neglect in the past, I deplore the present necessity of being compelled to fight with both the patient and his or her dentist for the removal of infected foci in the mouth. The dentist frequently will not cooperate. He naturally dislikes to remove his own fine handiwork. Hence, I repeat, when a bad

tooth comes out, or a dirty crown comes off, let the patient, or, if he is anesthetized, his nearest relative, smell of it. This is an educational propaganda.

CONCLUSIONS

1. Most unexpected tolerance to pyorrhea alveolaris and to tooth infection is found.

2. Chronic invalidism may be caused by mouth infections.

3. The blood pressure may be raised or lowered by mouth infections.

4. The thyroid gland is frequently enlarged, and may hypersecrete or hyposecrete, in these infections.

5. Serious disturbances of the blood, heart, kidneys, stomach, intestines and joints are frequent from mouth infections.

6. Glycosuria can be, and perhaps true diabetes mellitus may be, caused by mouth infections.

7. Serious distant focal infections may occur from mouth infection.

8. Serious brain and nerve disturbances, as well as neuritis, may occur from mouth infection.

9. Ulcer of the stomach, pyelitis, appendicitis and chronic colitis may be caused by pyorrhea alveolaris and mouth infection.

10. Pneumonia, especially that which follows influenza, may frequently be caused by pneumococci long carried in the patient's mouth.

11. No treatment of these conditions will be of any avail until the mouth is made clean.

12. Stock or autogenous vaccines are not very promising as to their therapeutic value, but in obstinate cases they should be tried. Therefore it is generally well to grow a culture from the infection in the mouths of these patients, that autogenous vaccines may be made and used, if desired.

13. One should be very careful not to promise a cure of a distant condition, although that condition was caused by the mouth infection. However, many brilliant cures are caused by surgical eradication of infected areas. The patient should always be told that the surgical removal of the infected area in the mouth does not remove the germ localized in distant parts of the body, nor does it immediately cure an inflammation caused by these germs in a distant part, nor will it restore degenerated tissue, but it will remove the primary source of infection.

14. It should be urged that any fresh lesion of the mucous membranes of the mouth is a source of danger, much as is a lesion of the skin. The efficiency of the integument in warding off disease germs has long been recognized. It should be recognized that fresh cuts, abrasions, and blistering of the mucous membrane of the mouth with iodin, or other strong escharotics, offer the opportunity for the absorp-

tion of germs that may be freshly received into the mouth, and more especially of germs already in the mouth.

I wish especially to thank Dr. George C. Fahy, a dental surgeon of New Haven, for his efficient scientific aid both in diagnosing the exact condition in, and in surgically eradicating, infected areas in the mouths of my patients.

SOME OF THE NEWER METHODS OF TREATING WOUNDS

BY FITCH C. E. MATTISON, M.D., F.A.C.S.,

PASADENA, CAL.

When requested by your program committee to prepare a paper on some of the "Newer Methods of Treating Wounds," I felt it was a task that could be done so much better by some of our members who have been at the front, and could give you their experiences in treating such wounds.

It is difficult for some of us to comprehend that in our age, when civilization has advanced to a point far beyond any that we know of, that any good can come out of the present conflicts; where weapons of destruction have become so mechanically perfect that the wounds inflicted by them are far more destructive, and conditions under which such wounds are made make infection almost certain, unless some benefits may accrue to mankind in the future by the necessity of the surgeon finding better methods in treating infected wounds.

It would be far beyond the limits of your patience to do more than mention some of the newer methods of handling such wounds. The present war has shown that sometimes necessity is the mother of invention, and when the soldiers commenced to burrow in the ground and sometimes were standing in mud most of the time wounds inflicted under such conditions were appalling. With clothing and their bodies covered with mud and trench filth, wounds under such conditions with splinters of shell, shrapnel, bullets, but especially pieces of clothing, were all infected. At first, such wounds were treated without regard for the possibility of tetanus, but it was not long before it became the rule to use tetanus antitoxin in all wounds.

In the Bradshaw lecture on "Wounds in War," Surgeon-General Sir Anthony Bowlby calls attention to the unfavorable conditions under which wounds are received. The country is thickly populated with human beings and supports many cattle and pigs; the soil is a rich loam, is heavily manured with excrements of men and animals; is covered by luxuriant crops; rainfall is copious; cloudy days are numerous, and every form of microorganism is abundant, and soil taken from a considerable depth below the surface bears pathogenic organisms. Men are covered by either mud or dust, and their comrades who help them are in a similar condition. Surgeon-General Bowlby speaks of the hypertonic salt solution of Sir Almroth Wright, and the use of antiseptics, and claims the object of each is the same in reality, for it is necessary for dead tissue to be disintegrated

or cut off, and sloughs and granulation tissue to grow before healing can take place. He also states that one can appreciate more clearly now than ever before why the older surgeons spoke of "pus laudabile et bonum." "They understood that when velvety granulation and creamy fluid appeared destruction had ceased and repair had begun; and we recognize to-day, as they did, that there is such a thing as relatively healthy suppuration."

The following is the plan, on which all agree, when a patient is admitted to a line hospital:

1. Removal of infected bits of clothing, or other infected foreign matter.

2. Wide incision and drainage.

3. Immobilization.

4. Continuous irrigation by drop method with Dakin's solution of sodium hypochlorite; English surgeons as a rule seem to prefer Wright's hypertonic salt solution with the addition of citrate of sodium (sodium citrate 1 part, sodium chloride 4 parts, and water 85 parts), or continuous immersion in antiseptic solution of acetate of aluminum.

5. Continuous exposure of all wounds when possible to avoid foreign body reaction.

Many antiseptics were tried, but the most satisfactory one so far seems to be Dakin's fluid. The details of the preparation were worked out in the chemical laboratory attached to the Rockefeller Foundation Temporary Hospital 21, at Compiègne, and were published by Dakin in the *Presse Médicale*. After many experiments with a large number of antiseptic substances, Dakin made choice of the hypochlorite of soda, which has high germicidal properties, with the advantage of being the least harmful to the tissues.

The preparation of a solution of suitable strength for direct application to the tissues, that is, containing from 0.5 to 0.6 per cent. of hypochlorite of soda, is very easily made. One hundred and forty grams of dry carbonate of soda, or 400 grams of the crystallized salt is dissolved in 10 liters of ordinary water, and to this solution is added 200 grams of chloride of lime of good quality. The mixture is well stirred up, and after standing for half an hour the clear fluid is siphoned off from the precipitate of carbonate of lime, and filtered through cotton wool. To the filtrate, 40 grams of boric acid are added, and the solution thus obtained is ready for immediate use. The boric acid in this solution is not added for its antiseptic action, but for neutralizing the alkaline reaction, which in itself is irritating.

Dakin claims no credit for the "new antiseptic." He states that it was discovered by a French chemist, Berthallet, in 1788, and used for bleaching and disinfecting purposes, four years later, 1792. Percy of the Javel Works near Paris, made a similar fluid, and sold it under the name

of eau de Javel. In 1820, Labarraque prepared a similar fluid which was known as Labarraque's disinfecting fluid.

This solution has been demonstrated by Alexis Carrel and his coworkers, Dakin, Dufresne, Dehelly, and Dumas, as being an energetic antiseptic solution, unirritating and of little cost. It should not, however, be used at the same time as alcohol, and must never be warmed. The solution should penetrate all crevices of the wound, and must be constantly renewed. After adequate drainage is provided, the solution is either forced into all portions of the wound, or the Murphy drip is used. The latter method has proven the most satisfactory.

Sir Almroth E. Wright's treatment of infected wounds by the use of hypertonic salt solution and vaccines, has met with some opposition from some of the surgeons at the front, and much of his work has not been correctly interpreted. He and his coworkers have worked out a very elaborate scheme for the phylacogogical treatment of wound infections. Briefly the scheme is:

At the First Aid Post after hemorrhage has been arrested, the wound has been cleansed, bandages, and splints applied, an injection of "antigangrene vaccine" is given. This is a vaccine containing the streptococcus, staphylococcus, and the bacillus of Welch. There would be, upon the inoculation, a rapid immunizing response, he claims, for all these wounds are infected, the predominating infection being the colon group. The most elaborate studies of these infections show that the clothing, bodies, and wounds of the men contain the colon group of bacteria.

Treatment in the field ambulance is: Washing and sterilizing, excision of projectiles and foreign bodies, procuring of efficient drainage, application of clean dry dressings, and injection of tetanus antitoxin. For the procuring of drainage, sufficient enlarging of the wound is made to permit of loops of sterile bandage previously steeped in a solution of 5 per cent. sodium chloride and 0.5 per cent. sodium citrate, these being carried down into the wound to serve as wicks. Previous to the introduction of the drain, the wound should be syringed out with the hypertonic saline solution. The ends of the wick are to be inserted between plies of lint well soaked in the same solution, and folded over so as to form a thick pad; one or two tablets of salt are planted in the dressing to keep the solution of proper strength when the lymph commences to flow, and over all an impervious protective dressing is placed. Wright claims that salt as a lymphagogue has no equal; 5 per cent. salt solution prevents clotting of blood, but not in the presence of pus, but the addition of the citrate of sodium prevents clotting of blood in the presence of pus.

Treatment at base hospitals consists of what he calls the full program of phylacogogic treatment. Cases of spreading infection, cellulitis, and gaseous gangrene are treated by free incision, supplemented by hypertonic salt solution until tissues are restored to their normal condition, and merely

the surface is irrigated with a physiological salt solution until all surface infections are extinguished, then secondary suture of wounds, then irrigation with 5 per cent. salt solution or Ringer's or Locks' solution (without the sugar). The use of antiseptics and antiseptic precaution in all wounds is insisted upon.

Sir W. Watson Cheyne takes issue with Sir Almroth Wright on the latter's suggestion of the importance of serum for infection. Wright suggests that the main value of antiseptics is due to their production of a flow of serum. Cheyne also objects to Wright's hypertonic salt solution of 5 to 10 per cent., and contends that "brine," as he calls it, is good to preserve dead tissue, but is bad for live tissue. Cheyne makes a plea for the principles of Lister in the treatment of wounds, and contends that of late years, "A most unaccountable prejudice has arisen against antiseptics, with the result that students have not been educated in their use; indeed have been taught to decry their value and to look on them as old-fashioned and very objectionable substances." Cheyne recommends a strong antiseptic, Lister's strong mixture 1/20 carbolic lotion, to which is added sufficient bichloride of mercury to form also a 1/500 bichloride solution, in the early stages; but uses very weak antiseptics, if any, in the later stages. He has had no experience with Dakin's solution, but favors borsal (equal parts of boracic and salicylic acid), or a paste containing carbolic acid or cresol and borsal. A review of the controversy between the old Lister school as represented by Cheyne, and the school represented by Wright, which has possibly lost sight of everything but vaccines and hypertonic salt solutions, would lead one to take the middle ground between the schools.

Browning and his coworkers at the Bland-Sutton Institute lay down what they regard as the essential qualifications of a useful antiseptic. The bactericidal substance must have a great potency against all organisms in the presence of protein material, such as serum; it must be stimulating to granulation; it should have no deleterious effects on phagocytosis, no irritating action on tissue, and no toxic effect on the more highly specialized cells.

They found that a number of acridine dyes have an enhancing bactericidal power in the presence of serum and amongst these, the compound diaminomethyl-acridium chloride, which the authors, for the sake of convenience call "flavine," stands out foremost. This substance has been found to be 20 times more powerful than corrosive sublimate and 800 times more so than carbolic acid under these conditions.

Flavine and brilliant green are the two substances which hitherto have given the highest "therapeutic coefficient"; or in other words, the higher the germicidal power of a substance in the presence of serum, and the lower the effect in inhibiting phagocytosis, the more valuable that substance is as an antiseptic.

A practical formula for estimating the value of wound antiseptics, of arriving at their "therapeutic coefficient," as they put it, may be obtained by taking the ratio between (1) the highest concentration of the substance which does not reduce the phagocytic count below half that of the control, and (2) the weakest concentration of the substance which is sufficient to kill staphylococci in the presence of serum.

Delbit of Paris recommends a 12 per cent. solution of magnesium chloride for irrigation, for dressings, and for subcutaneous injections. This fluid has over ordinary antiseptics the advantage of respecting the cells.

Rosenblith reports an analogous method. He had originally made use of magnesium chloride in the form of hypodermic injections of a solution containing in each c.c. 0.25 gr. of magnesium chloride and 0.02 of sodium iodide; later he used a stock solution prepared by dissolving 250 grams of magnesium chloride in one liter of boiling water. For use, 4 tablespoonfuls of this are added to sufficient boiling water to make up to one liter, which is the normal solution employed at the Hospital Janson.

Dr. W. J. S. Ingram of Aberdeen, in deep infected wounds, uses silver nitrate stick very thoroughly and follows this by hot fomentations, and claims the wounds so treated clean up more quickly than after any method he has tried.

C. W. Duggan of Lincoln, England, uses equal parts of ichthyol and glycerine, this he applies with a camel's-hair brush, painting the surrounding skin as well as the wound.

The brilliant results obtained in the treatment of face and head injuries are due in no small part to some of the French surgeons whose patience and skill have won for them the admiration of the world, and when the history of this great European conflict is written, the French surgeon will share with the French soldier the praise they have so justly won.

When the surgeon of a few years ago had an un-united fracture or a comminuted fracture to operate on in a modern well equipped hospital, and got a satisfactory result, he felt justly proud of it, but consider the brilliant results obtained by some of the war surgeons, with badly shattered limbs in patients who are physically exhausted, with all conditions to make infection, and operating under conditions that are not ideal. Confronted with conditions such as they found, the surgeons had to meet difficulties such as are rarely, if ever, encountered in the usual run of hospital cases, where aseptic rather than antiseptic surgery is the rule, and where such wounds are taken to the hospital without delay.

Clinically the surgeons at the front who have paid close attention to thoroughly cleansing all wounds of all foreign substance, then rendering those wounds as free from infection as is possible, followed by thorough drainage by whatever means seemed best to them, have gotten good results; and if combined with all such means, a vaccine can be made for

that particular case, we can all agree that the injured man is at least having all means known to science used for his benefit.

Capt. A. L. Lockwood of London has treated a large number of gunshot wounds of the knee joint along new lines. The cases he reports were admitted from two to five days following the injury. Where there is effusion, the joint is tapped and the fluid withdrawn to relieve tension, and if the fluid is blood stained or perceptibly purulent, he injects a 2 per cent. formaldehyde solution in glycerin (made up at least 12 hrs. before and not more than 7 days old), about 2 drams being used; or he employs ether and iodoform, pure ether, or 5 per cent. saline solution. The aspirated fluid is examined, the knee is immobilized, and screened or skiagraphed in two planes at right angle to each other. After it is determined to what extent the knee is injured, and the degree of infection, then the wound is excised *in toto,* and with another knife and forceps the capsule is excised, this knife and forceps being at once discarded; then, no necrotic tissue being left, and all foreign matter having been removed, all blood clots are irrigated out with saline solution. The capsule is stitched up, and drainage is made down to the capsule, but never in the cavity of the joint. Much tension is never allowed in the joint, but aspiration is made before tension becomes too great. Great care is taken in properly splinting all cases.

The points on which he lays most stress are: (1) That all foreign bodies, whether metal, loose bone, or clothing, should be removed from the knee joint at the earliest possible moment. (2) Perfect immobilization is absolutely necessary, do not start passive motion too early, wait at least three weeks after inflammation has subsided. (3) Absolutely complete excision of all necrotic or even edematous tissue. (4) The capsule should be closed at the first operation if at all possible. (5) Antiseptics other than those mentioned are never introduced into the joint. (6) Tubes should never traverse the joint surface.

W. Hale White of London calls attention to the low mortality of bullet wounds of the chest. According to Col. L. A. Lagarde, U. S. A. (Gunshot Injuries, 1914), the mortality of penetrating wounds of the chest in the French army during the Crimean War was 91.6 per cent., in the English army, over 70, and among those which survived to reach hospitals in the American Civil War was 62.5 per cent. But with the introduction of small bullets of high velocity, it began to fall. Thus in the Spanish-American War it was 27.5 per cent., in the Boer War 14 per cent., and among the Japanese in the battle of Mukden 3.67 per cent.; in the present war, although the mortality is low, it is probably not as low as the last figure.

Lieut. Col. A. Primrose, Canada General Hospital, does not favor Sir Almroth Wright's plan of treating septic wounds by applying a 5 per cent. solution of sodium chloride and a 0.5 per cent. solution of sodium citrate, and applying a covering of "impervious protective tissue," as it hampers

drainage by preventing a free evaporation from the surface and absorption into the dressing.

Col. A. W. Mayo-Robson contrasts the experience of treating gunshot wounds of the abdomen during the South African War, where it seemed to have been proven conclusively that opium, starvation, and rest in the Fowler position yielded better results than operation. His experience while serving in the Dardanelles, was that the wholesale expectant treatment was a failure. Where cases were seen late, and peritonitis had developed, he found that a small incision over the pubes, and the placing of a drainage tube, the patient being in the Fowler position, was the best treatment. He states that similar treatment is the best for typhoid perforation, as a good proportion of such cases are being saved in one of the large typhoid hospitals in France.

Dr. George W. Crile uses Winchester Doubouchet's method of treating wounds by the use of Dakin's solution and electric light. Crile uses bell-metal hoods or pasteboard cones. Electric lights are placed in these of a sufficient candle power to feel comfortable to the patient, and the results are very gratifying, infected wounds are exposed to the light without dressing, and wound secretions are cleansed with Dakin's or Wright's solution.

The writer has had very good results with this method, and especially in the treatment of extensive burns, and in skin grafting following burns. The wounds dry up very quickly under frequent cleansing with acetate of aluminum solution when there is too much moisture, or the use of Wright's solution to promote secretions when such wounds become too dry from lack of serum.

Dr. Rutherford Morrison of the Northumberland War Hospitals has used a paste composed of iodoform 2 ounces, bismuth subnitrate 1 ounce, liquid paraffin q. s.; any consistency may be made, but the most useful are those of soft butter or thick cream. All gangrenous and necrotic tissue is cut away, and the wound swabbed out with alcohol and a small portion (not to exceed 2 drams) is vigorously rubbed into the tissue, a little being left in the bottom of the wound. No dressing is required for 7 to 14 days. He claims that (1) this paste maintains a continuous antiseptic action in the wound. (2) It acts as a lymphagogue and a free exudation of serum washes the wound from within outwards. (3) It does not prevent the escape of discharge. (4) Granulation tissue grows freely in contact with it. (5) Drainage tubes and gauze drains are unnecessary. (6) Septic wounds heal nearly as rapidly as non-infected ones. (7) Bone union is rapid and the tendency to form sequistrum is slight. Both constituents of the paste are toxic if absorbed freely, hence the use of more than 3ii of the paste may prove toxic.

F. C. Lewis of the University of Liverpool produces hypochlorous

solution electrically from hypertonic salt solution. He describes a very simple apparatus for its production from sea water and claims it is much more potent than the solution as ordinarily made, and wounds treated with the solution produced by electrolysis have given better results.

Sauerbruch, at the Swiss Surgical Congress in 1916, narrated his surgical war experiences in Germany, and is convinced of the necessity of immediate operative interference in all gunshot wounds of the abdomen; in which the peritoneum is involved, and believes that when this necessity is generally recognized, the arrangements for carrying out the operations will readily be improved at the front.

Dr. John O'Conor of Buenos Aires reports excellent results in the treatment of infected wounds by four-hourly irrigation with hot peroxide solution (2 ounces to the quart), followed instantly by hot carbolic acid lotion (½ ounce to the quart), followed by perchloride of mercury fomentations (wrung dry).

In going over the literature of the modern treatment of wounds, one is struck by the fact that there are two schools, or one may say factions. One which may be called the antiseptic school pins its faith on the use of some antiseptic, and there are many of these, with various combinations.

The other school, led by Sir Almroth Wright, the "Concentrated Saline School," depends for its success upon the fact that every precaution is taken to favor the rapid removal of all discharge from the wound by the hypertonic salt solution and a "salt pack." This pack, it seems, might be hurtful if one followed the directions by putting salt tablets in the dressings to be dissolved by the discharge from the wound, and in this way maintain the saline strength in the dressings. Might not such a "pack" act to dam back secretions from the wound, and prevent drainage? "Hot packs" of any sort, Dakin solution, hypertonic saline solution, or even sterile water, if such "packs" are changed frequently, not only facilitate drainage, but help to maintain adequate circulation and prevent lymph blocking. If any such hot pack be used and not used too long, drainage is facilitated. On the other hand adequate drains in a wound with a moderate amount of dry dressings that do not prevent drying of the wound quickly, are both rational and efficient.

Both schools agree thoroughly that all infected material must be removed from the wound, that drainage must be thorough and to all parts of the wound, and that such drains must drain the wound and not leave pockets; that drains, either tubes or gauze wicks, must be so placed that no obstruction is left to the free exit of secretions; that the antiseptic used must not be so strong that coagulation of the discharge takes place or irritation is caused; that, where practicable, wounds should be left open and not covered with thick heavy dressings that

might by their saturation with the discharge act as a "pus poultice" and obstruct such discharge, clogging up lymph spaces, and favoring absorption rather than elimination of wound secretions.

The middle ground between these schools seems the most logical, as they both aim at the same ideals and for what surgeons have been striving for these many years, free mechanical drainage to all portions of the wound. If frequent irrigation of the wound by some solution that does not irritate tissue, and that is mildly antiseptic, will accomplish better mechanical drainage than will drainage tubes or wicks, such irrigation should be used, for war surgery differs from civil surgery only in so far as it is different in degree and character.

The handling of large numbers of cases under unfavorable conditions, necessitating prompt and efficient drainage, seems to have been met by both schools. They do not differ much in results. It seems to many of us that there are middle grounds between these schools that will prove of inestimable value; that the ingenious methods devised to procure adequate and prompt drainage and to maintain such drainage until all infection has been removed, are used by all.

The selection of an antiseptic to be used in a wound is only one factor, but the way it is used is essential to its efficiency. Carrel claims that the rapid washing out of a wound with the strongest antiseptic and keeping the agent in contact with the infected area for a few minutes only, produces little or no results, and sometimes the application of strong antiseptics does harm rather than good, for if such agent produces coagulation of wound secretions or necrosis of tissue harm will result.

There are many problems in the treatment of wounds that are being worked out from a matter of necessity and so far it does not seem possible to use any of our present antiseptics in strong enough solution to sterilize wounds thoroughly by a few applications without producing either a coagulation of the wound secretions or necrosis of tissue, which favors bacterial growth.

The most effective way of treating such wounds is to use weaker antiseptics that limit bacterial growth and do not irritate, but constantly cleanse the wound of all material favoring bacterial growth. The problem of reaching such wounds through the blood stream either by a vaccine or chemical agent has not been solved, but the downfall of autocracy may bring with it the downfall of the autocrats of wound infection, and although the price in human life seems appalling to us now, future generations may reap some benefits in the conservation of human life by the handling of wound infections.

TREATMENT OF CHRONIC BRIGHT'S DISEASE

BY J. M. ANDERS, M.D., LL.D.,

PHILADELPHIA, PA.

There are two principal criteria which should serve to guide us in the treatment of chronic Bright's disease. They are, the general condition of the patient as it is influenced by the progress of the affection, and the rate of metabolic excretion as determined by modern methods of examination. We should also pay due regard to the results of clinical and microscopical studies of the urine, although in my experience both albumin and tube casts have, at times, shown a tendency to increase under a judiciously restricted diet on the one hand and to remain uninfluenced by a pretty generous diet on the other.

Without stopping to attempt to remove the touch of vigorous professional confidence in the percentage of albumin and the number and variety of tube casts as an index to the severity of the morbid process, and making it the foundation for prognosis and treatment, I feel that we have depended too exclusively on this somewhat uncertain standard in the past.

I propose considering the two criteria mentioned above for a moment separately so far as practicable, believing that most light may be thus thrown on the present-day means of dealing with this important disease.

The Rate of Metabolic Excretion.—This must be gauged by the most modern and approved methods. The amount of urea excreted in the twenty-four hours is an indication of the outcome of the case, and should be carefully and repeatedly estimated.

Among the substances excreted with great difficulty by a diseased kidney is creatinin. In this connection it is of interest to note that Myers and Lough have shown that an estimation of the blood creatinin is of prognostic value, *e. g.* over 5 mg. per 100 c.c. of blood having invariably terminated fatally in from a few days to two months, while figures from 3 to 15 mg. are to be regarded as decidedly unfavorable. It is essential, therefore, that substances which like urea, creatinin, pigments, hippuric acid, and phosphates are excreted with difficulty, should be allowed in minimal amounts in Bright's disease. To avoid the ill effects of phosphoric acid, von Noorden[1] recommends that calcium carbonate be added to substances containing it.

The test meal for renal function probably gives the earliest evidence of diminished kidney efficiency. Mosenthal and Lewis[2] hold phenol-

sulphonephthalein excretion and Ambard's coefficient are tests which enable one to follow most minutely the progress of renal disease.

General Condition of the Patient during the Progress of the Disease.—While seeking to afford protection to the diseased kidney by extreme moderation in diet, especially in proteins, due attention is to be paid to the matter of avoiding deleterious effects to all other organs—to the metabolism. The strength of the patient is to be preserved by adapting sound hygienic, therapeutic, and dietetic principles to the individual case.

Extremes of mental and bodily activity are to be avoided and the habits and mode of life of the patient regulated, the aim being to maintain the nutritive equilibrium, without producing irritation of the renal epithelium. All noxious substances entering into the etiology must be avoided and removed as far as possible. Primary foci of infection, *e. g.* in the teeth and tonsils, or elsewhere, should receive particular attention. By diminishing or removing such irritants as uric acid, alcohol, lead, and the like, the cardiovascular system is also conserved—a point of vital importance. The cooperation of the patient is always necessary to the end that the directions given shall be carried out persistently and faithfully.

The value of a change of residence to a warm, dry, and mild climate in many cases of the chronic interstitial form of Bright's disease is undoubted. The variability and humidity of temperate climates, particularly during winter, are aggravating factors in this disease, while a sea voyage or a sojourn at some resort where the soil is dry and sandy, and the climate warm and equable, may be highly beneficial.

Diet.—The chief control of chronic Bright's resulting from treatment is found in diet coupled with the foregoing suggestions pertaining to mode of life, rather than in drugs. The dietary restriction should be both quantitative and qualitative. I quite agree with Shattuck[3] that a varied diet is more likely than a monotonous one to promote the making of good blood and improving the general nutrition, and that of the myocardium in particular.

An excess of protein, which is always harmful, can be avoided only by a close study of the functional capacity of the kidney at short intervals of time, and the repeated estimation of the urea and creatinin content of the circulating blood. By pursuing such a course it is found that ofttimes greater latitude may be extended without injury to the sick kidney, and thus aid decidedly the general metabolism. In this connection, the view of Foster and Davis[4], to the effect that in cases in which there is no great amount of edema, we must allow considerable water, the while we diminish the protein intake, in order to eliminate the solids and retained nitrogen, is sound and to be adopted.

On the other hand, when dropsy of a more marked degree is present,

the fluid intake should be restricted to a total daily amount not exceeding one liter. In this class of cases, composed largely of instances of chronic parenchymatous nephritis, a salt-free, or, what is more practicable, a salt-poor dietary, is a most useful adjuvant to efforts at removing the edema.

While whole milk should make up a considerable portion of the diet, von Noorden has pointed out that milk contains on the whole too much protein, and recommends that it should be restricted to three pints a day, to which a pint of cream should be added. The writer has found skim milk and buttermilk, in appropriate quantities, of signal value in cases in which dropsy is marked.

Recently, Terwaert and Van Lier[5] have put forth the claim, based on their experiments and clinical experience, that restriction to a milk diet in cases of nephritis with retention of urea is decidedly harmful.

In general, a mixed diet will be of advantage; proteins in quite limited amounts,* greens, fruits (especially fruit juices), pure fats, and light, well cooked farinaceous dishes and cereals (except oat-meal) may be allowed. Cocoa may be allowed as a beverage at the morning meal. The effect of a given restricted dietary is to be noted by making careful observation of the bodily weight and of repeated tests of the functional capacity of the diseased kidney as well as of the urine and urea and creatinin content of the blood.

In the writer's view, it is no less important to the welfare of the sufferer from chronic Bright's that the metabolic processes be watched than to protect by an appropriate diet the chronically "sick" kidney with a view to maintaining, as far as possible, its functional equilibrium.

Drugs.—Drugs, while not curative, may counteract certain dangerous tendencies resulting from interference with kidney excretion. In the exudative variety, in which anemia is often pronounced and progressive, a chalybeate course, from time to time, is useful. In this form, anasarca is also present and calls for treatment. The patient should be put to bed, where he should remain until the circulatory equilibrium is restored, while, at the same time, cholagogues, diuretics, and diaphoretics should be given.

Saline cathartics, exhibited after the Matthew Hay method, *e. g.* in concentrated solution in the early morning, so as to produce two or three watery discharges daily, are useful. Mercury, in all of its forms, is to be omitted, since it has been shown that this drug has a selective affinity for the kidney and is, therefore, harmful in its effects in Bright's disease. Unfortunately, the custom of prescribing a mercurial preparation at intervals in this complaint, especially when edema is present, is

*While from 80 to 100 gm. of nitrogen daily are required, it is often advisable to allow much less, even as small an amount as 5 gm. for a week or two.

only too common, but it should not be approved by the medical profession.

Again, one of the main aims of treatment is to spare the renal epithelium, irritating substances, hence such diuretics as caffeine, theophylline, sodium-acetate, and other members of the purin group should be abandoned in the therapeutics of this disease. On the other hand, we may employ for their diuretic effects, unirritating substances such as digitalis and the salts of potassium, especially the citrate, either singly or in combination.

Active diaphoresis, especially if induced by means of hot water baths, or hot, wet or dry packs, is a potent factor in lessening dropsical transudates and the albuminuria, if persistently carried forward at intervals of twelve or twenty-four hours.

In cases in which the renal lesions have not reached an advanced stage, the writer has observed excellent results from a course of the hot Nauheim baths, which markedly enhance elimination through the skin and kidneys.

The Karell diet, or the Karell cure, is warmly advocated by Goodman[6] and others. The technique is simple: "The patient receives daily at 8 and 12 a.m., and 4 and 8 p.m., 200 c.c. of raw or boiled milk, warm or cold, according to the taste." If great complaint is made of thirst, the patient may be allowed to rinse out his mouth with water, with instructions, however, that none be swallowed. It is customary to continue this strict diet in cases of renal edema for a period of one week, after which it may be gradually relaxed.

No aspect of the therapeutics of Bright's disease has engaged the attention of the profession to so great a degree as that of the associated hypertension. The lesson has not been learned as yet when active interference with this ofttimes compensatory mechanism should be commenced. It is to be recollected that while high systolic and diastolic blood pressures are constant symptoms of chronic interstitial nephritis, if we except the arteriosclerotic kidney of the aged, the inflammatory parenchymatous form, so long as it is compensated, exhibits no increase of blood pressure.

Says Engel[7], the theory that ascribes nephritic hypertension to the chronic parenchymatous variety of renal disease rests upon confounding it with cardiac hypertension. In approaching the question of the management of the symptom, it is well to keep in remembrance that in the renal type of high tension, including evidences of damage to the vascular system, an unfavorable prognosis appears to depend, as pointed out by Stone, upon the height of the diastolic pressure, to which rather than to the systolic, our closest attention should be given, since it should form a guide to aid our efforts to reduce high blood pressure. In view of the presence of a greatly increased diastolic pressure, myocardial exhaustion supervenes, re-

sulting in decreased urinary output, and symptoms due to increased retention of urea, leading in some cases at last to a fatal termination.

On the other hand, cerebral deaths, due to the greatly augmented diastolic pressure, are more common than myocardial deaths. It follows as a natural corollary that by a reduction of the high diastolic pressure, we not only relieve such features as headache, vertigo, and so-called renal asthma, but also and more importantly, prevent rupture of the cerebral arteries—an accident that often terminates life abruptly. This indication is to be met by the cautious use of nitroglycerin in ascending doses, beginning with 1 minim every three hours. In this manner we also relieve the heart of a serious strain, which is the result of a greatly increased tension and may lead to myocardial exhaustion. My experience of the use of hot baths in selected cases accords with that of Rowntree[8], who states that a drop of 10 to 20 mm. often persists some time after a hot bath that results in a good sweat.

While affording therapeutic assistance to meet high tension, the effects upon the heart, the urinary output, and the urea and creatinin content of the blood must be noted. A too great reduction of the arterial tension, a prevalent mistake, is undesirable, being attended with danger of uremia and serous transudates owing to the resulting insufficient urinary excretion.

Myocardial exhaustion, which manifests itself in the terminal stage of cirrhotic kidney, with signs of cardiac dilatation, scanty albuminous urine, and anasarca, requires heart tonics and stimulants. Here digitalis has good effects; it improves the myocardial tonus and often decidedly increases the urinary output as to both fluids and solids for a season at least. With the digitalis, a small dose of nitroglycerin may be combined if the peripheral tension be high.

If, despite the treatment described above, definite uremic manifestations, more particularly vomiting, muscular twitching, convulsions, or coma, supervene, vigorous measures are to be resorted to with all possible expedition. Starvation for two or three days is advisable. Prompt venesection followed by the use of physiological salt solution given subcutaneously, 500 to 1,000 c.c., as recommended by Herrick[9], often gives much temporary relief.

The writer has observed good effects from the subsequent employment of the Murphy drip method of administering this solution, preceded by colonic flushing. Free catharsis and active diaphoresis must be secured in the manner above described.

Inhalation of chloroform, or, what is often a useful and the writer believes an essential measure, in some cases at least, the hypodermic injection of morphine in doses of from gr. 1/6 to ¼, is to be employed, and repeated according to the indications of the particular case. White and Wilcox[10] have shown that morphine does good in Bright's disease, by diminishing the oxidizing functions of the body metabolism. The late Dr. LeFevre

lauded chloral, and the writer has observed gratifying results from its use in half-drachm dosage thrown into the rectum at intervals as required.

Time and space do not permit of a full presentation of the treatment of all complicating conditions and symptoms in chronic Bright's disease, but those omitted from consideration here must receive attention in accordance with accepted therapeutic principles.

Kidney Organotherapy.—This method of treatment has recently received considerable attention, but it has not had vogue long enough to permit of a proper appreciation of its value. Sajous[11] claims that favorable results have been reported in about one-half of the cases of chronic nephritis in which kidney preparations have been tried. One may use a maceration, as have Page and Dardelin[12], or, more conveniently, a tablet preparation. The dose of the latter is ten to fifteen 5-gr. tablets daily, preferably given between meals. Kidney preparations produce several effects of which the chief are three: (*a*) The prevention of uremia, (*b*) a reduction in the percentage of albumin, and (*c*) increased diuresis. It is not improbable that kidney preparations owe their stimulating effect upon the urinary output and their antitoxic power to an adrenal principle in organic combination.

Salvarsan has yielded encouraging results in cases of syphilitic origin. Perhaps the only prerequisite to a fair degree of success in the use of salvarsan or neosalvarsan is the selection of cases in the earlier stages of this form of nephritis, since no drug "can possibly restore destroyed renal parenchyma or transform fibrous connective tissue into secreting kidney cells."[13]

Surgical Treatment.—The percentage of cases in which surgery, *i.e.* incision of the capsule or cleavage of the cortex, serves a useful purpose is probably small, and it is gratifying to note that the ardent advocates of these operative procedures are far less numerous than they were a single decade ago. It is conceivable that a splitting of the capsule or mere puncture of the same will diminish abnormal tension and thus relieve pain which may be present. Moreover, for hematuria, more particularly if practically limited to one side, "the operation should be recommended, as it has been frequently followed by the cessation of the hemorrhage in chronic Bright's disease." (Newman[14].)

As a rule, the good effects of operation are only temporary, the result of an improved circulation which, however, cannot be long maintained. Surgical methods cannot modify the nature and progressive character of a chronic nephritis, cannot arrest nor even appreciably retard the renal and arterial fibrosis and their mechanical consequences. Finally, no form of treatment is, in a real sense of the word, curative that has not for its main aim an amelioration of the toxemic condition present and the removal of etiological factors in particular cases.

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DISCUSSION.

Dr. Cornwall said that in the treatment of chronic Bright's Disease the main thing was easement of the work of the crippled kidneys. This obviously was effected chiefly by regulation of the diet, and especially by regulation of the nitrogenous ration, qualitative as well as quantitative. It was not enough to reduce the amount of protein to the minimum health ration, or even to interpose periods of protein starvation; it was necessary also to select the protein-containing articles of food with the object of getting those whose metabolism would be attended with the by-production of the minimum amount of protein fragments of deletrious charcter, or those that are poorly eliminated, such as fragments of the purin class and the leucomain and ptomain class; which practically meant a diet from which animal food, with the exception of milk and its products, was largely excluded. The necessity of keeping down the quantity of the undesirable protein fragments in the diet of chronic nephritics could not be too much emphasized. The prophylaxis of chronic Bright's Disease was a phase of its therapeutics which deserved more attention than it usually received. The need of this prophylaxis was often suggested by heredity. And the most important thing in this prophylaxis was the early adoption of the easy nitrogenous diet.

Dr. Wood: Dr. Anders has spoken of the dangers of the injudicious use of calomel as a diuretic, in nephritis; I should like to go a step further and call attention to the possibility of injurious effects from any diuretic. It is to be remembered that we are dealing, essentially, with an inflamed organ and any increase of functional activity is liable to add to the degree of damage; rest is what we need, not increased function. The investigations of Dr. Christian have shown that in experimental nephritis in the lower animals, death is hastened rather than delayed by the use of diuretics.

In regard to the lowering of the blood pressure I think it is well to bear in mind that many of these cases need an arterial pressure somewhat higher than what we call "normal" and it may be a mistake to try to reduce the pressure too much. When it is deemed desirable, however, to lower the pressure, I should like to call attention to the value of an old remedy that I did not hear Dr. Anders mention and that is Veratrum Viride. Since this drug acts by slowing the heart it tends to conserve cardiac energy and, I believe, is less liable to cause too great a fall than are the Nitrites.

IS GASTRIC ULCER AN EXANTHEM OF ALLERGIC ORIGIN? IF SO, WHAT IS ITS TREATMENT?

BY ROBERT T. MORRIS, F.A.C.S.,

616 MADISON AVENUE, NEW YORK.

The term "exanthem" in common acceptance relates to the external cutaneous covering. In the embryo the mucous surfaces arose from the endoderm and the skin from the ectoderm. Both of these surfaces are covered by an epithelial layer. If we picture the mucous surfaces as well as the skin surfaces as still being akin to each other, we may in that light take up the question of gastric ulcer as an exanthem, corresponding to some of the skin diseases. Certain ones among the skin diseases are of allergic origin. Sensitized patients make allergic response to various toxic processes manifested in localized irritative or destructive influence upon skin cells. It is my belief that gastric ulcer belongs in the same category. Rosenow has explained to us the nature of elective affinity of certain tissues of the body for certain poisons. In some of the skin exanthemata, there is elective affinity for certain toxins, and these toxins concentrated at elective points produce irritative or destructive influence in two chief ways. First, by direct toxic influence; next by over-action of antibodies called out by the presence of toxins.

Now let us carry this same principle to that other part of the ectoderm which became the mucosa of the gastric area. We know that the part of the mid-gut represented by the pylorus and the duodenum particularly, possesses elective affinity for certain toxins in high degree. Why does one patient carrying toxins of a certain sort in his blood circulation develop ulcer in the gastric area, while another patient carrying still more of the same toxins in his blood circulation has no such ulcer?

For purposes of argument we may assume that the patient who has the ulcer has been sensitized. In other words his ulcer is of allergic origin and corresponds to an exanthem of the skin. Many years ago before the subject of elective affinity had been presented to the attention of the profession, I showed that the appendix vermiformis was the seat of peculiar toxic demonstration, different from that occurring elsewhere in the intestinal tract. There was not only direct toxic destruction of cells but a proliferative endarteritis frequently closed the blood vessels of the appendix and cut off the circulation of part or the whole of its terminal arterial system. Later I found that the same pathologic phenomena occurred in ulcers of the gastric area, where we likewise have terminal arterial anatomy. We know

that because of elective affinity for toxins in the gastric area, this part of the modified ectoderm undergoes destructive processes.

Sometimes there is widely extended injury to superficial capillaries in such a way that we have a "bleeding sponge" ulcer, hardly to be classified as ulcer because the defect is not much in evidence on macroscopic examination. In other cases there is proliferative change in the tunica intima of blood vessels belonging to one or more terminal arterial groups. Because of the resulting localized anaemia, the anaemic tissues have lost their defence mechanism against bacterial inroads and against digestive processes. In such cases we have a localized indurated ulcer or a perforating ulcer caused by direct toxic influence, by over action of antibodies called to that region on account of the presence of the toxin, or we have further a third element of bacterial inroad upon anaemic tissue, or still further a fourth element of peptic action upon tissue which has been deprived of its defence mechanism.

If gastric ulcer is an exanthem of allergic origin what is its treatment? In the history of medicine the treatment of disease conditions has been at first a matter of alleviation of symptoms. Symptomatic treatment of any illness belongs in category with superstition in religion. Superstition takes the place of knowledge pending the time when knowledge may be acquired. Now that we have acquired knowledge of the subject of elective affinities and we have become familiar with the fact that toxic influences are fundamental in cases of gastric ulcer, a critical examination of the subject from its fundamentals allows us to conclude that the treatment of gastric ulcer must begin from the treatment of the condition or conditions responsible for the production of toxins which make the round of the blood and lymph circulation.

INSTITUTIONAL TREATMENT OF DISEASE AND SPECIALIZATION

BY FRANCIS M. POTTENGER, A.M., M.D., LL.D.,

MONROVIA, CALIF.

Efficiency in therapeutics concerns not only the remedy but the manner in which, and the conditions under which, the remedy is applied.

The advances in therapeutics which have been made during the last few years have not been confined to finding more efficient remedies. Much attention has been given to better application, and the conditions under which the patient is treated are ever receiving more and more attention.

Out of this study has sprung the institutional treatment of disease. It is within the memory of the present generation when institutions were only for the poor and helpless. Their fields of application, too, were limited to very few diseases. To-day, however, the sphere of institutional treatment is being extended to almost all severe, serious diseases.

When scientific medicine was young and little was known of the nature of even the most common affections, institutions were considered as necessary only for those whom the municipality and state felt an obligation to look after when ill. The public hospital was almost alone save for a few institutions for the care of the deaf and dumb, blind, imbeciles, epileptics and mental cases. It is impossible, however, for such a big idea as that of institutional treatment to be long confined to narrow limits. The idea that the poor who were treated in institutions received more efficient medical service than the wealthy who were treated in their homes, was gradually grasped by the medical profession and then seized upon by laymen.

One of the greatest factors in advancing the institutional idea has been the wonderful development of surgery. Surgery has demanded certain facilities and conditions which can best be had in permanent institutions. While the surgeon can carry his operative equipment with him from place to place, yet operations can be done so much easier and so much more successfully, and there are so many more operations that can be done safely, in the permanent, suitably equipped operating room, that the operation in the home is now almost unheard of. Surgery could not have advanced as rapidly as it has without the aseptic surroundings and improved facilities of the modern hospital. Thanks to it, no cavity of the body to-day offers barriers against surgical skill. Operations can

be performed in the home, but they are done so much more successfully in the hospital, and the mortality rate and the term of illness has been reduced so substantially, that one no longer doubts the advantages of the hospital as compared with the home in surgical affections.

Careful observation shows that the better surgical results obtained in hospitals are not alone due to the operating equipment and improved surgical technic carried out; but are also due to the fact that the patient is removed from the harmful influences of the home and given the assistance of trained attendants. This then is the true hospital idea, an institution constructed and equipped for the treatment of a special class of cases, manned by special attendants not only trained in the mechanical application of measures, but also to provide the particular helpful atmosphere that is necessary for the patients. This idea is applicable to all diseases.

Efficiency is the watchword of business enterprise. The aim is to produce the best result at lowest cost. This is just as applicable in matters of health as it is in things material. The public, however, has not yet learned this. Health is more valuable than any product from the mine, field, or shop. Each ablebodied individual has a productive value. He presents a certain investment which has been necessary to bring him to his existing state, and, further, he represents potential energy which may be utilized in the production of wealth.

Disease is the foe of efficiency. Morbidity not only decreases efficiency, but causes waste in that it calls for increased outlay. Every time a man is ill, the capital which is sunk in his business is increased by the expenditure required to restore him to health, plus the loss in earning power during his illness, and, at the same time, his future productiveness is in many instances decreased. Economically, then, we have an increased investment with diminished returns. Here then is the economic argument for the efficient treatment of disease which requires not only that the best therapeutic measures be supplied, but that they be applied under conditions which are most favorable. Everyone recognizes the difference in waste between systematized and unsystematized production. Vast fortunes have been made simply through the elimination of waste. The same difference exists between organized, systematized treatment of disease as represented in properly constructed, equipped, and conducted institutions, and treatment in poorly managed homes. No great fortune is piled up by any one, but the saving is distributed to many. A few days of idleness saved here, a few weeks and a few months saved there; a greater efficiency here, a life saved there. Such results are not as plainly seen as an accumulation of visible wealth, but they are just as certain and far more remunerative to the public at large.

It must also be understood that institutional treatment in itself does

not guarantee efficiency. It may be more wasteful than treatment in the home. Much depends on what might be determined "the soul of the institution," that is, "the atmosphere about it"—the thing which can not be defined, but which impresses one on entering it. When right, it is helpful and inspiring; when wrong, it is harmful and depressing. Too great a proportion of the total concern for institutions is paid to construction and equipment and not enough to creating an optimistic, helpful atmosphere. Brick and mortar make the visible structure, but the "atmosphere" is the real soul created by those who are responsible for its policies and who conduct its operation. This is particularly true of institutions for convalescents and those suffering from chronic disease. It might be said that construction and equipment are most important to acute medical and surgical affections; but, even in these no one will doubt the influence that a cheerful and hopeful atmosphere has in stimulating the body defenses for the serious ordeal of an operation, or for withstanding the harmful influences of acute disease. There is a central nervous system back of every patient suffering from disease, whether surgical or medical, and when this is shielded as much as possible from harmful stimuli, the patient is aided most.

The institutional idea is growing. In the future it will probably develop faster than in the past; and, while not wishing to prophesy, yet I will assert that the institutional treatment of disease will be successful in proportion to the success that it meets in furnishing the helpful atmosphere demanded by those who are ill.

I elsewhere detailed some of the difficulties which are to be overcome in order to make the home treatment of tuberculosis as successful as institutional treatment (Clinical Tuberculosis, II, p. 470) and since the principle underlying treatment of all diseases is much the same, I shall quote from that discussion:

"The home treatment of tuberculosis will be successful in direct proportion to the manner in which sanatorium principles are established and carried out. By the term 'sanatorium principles' is meant a carefully planned program of hygienic living, personal hygiene, regulated rest and exercise, food prescribed to suit the needs of the patient, and other measures which are directed toward increasing the patient's vitality, and surrounding the patient with an atmosphere of cheer and hope.

"There are two things to bear in mind in treating the patient in the home: first, the arrangement of the room, or whatever accommodations are occupied by the patient in such a manner as to afford the greatest aid to recovery; second, the training of the patient so as to avoid scattering infection and transmitting the disease to others."

and again (p. 472):

"After accommodations have been supplied to the patient in such a way as to afford him the best application of the open air life possible under the circumstances, the next important problem is to furnish him with helpful surroundings. The difficulty here is that the patient is the exception. Home activities are intended for the well. It requires sacrifices not only on the part of the patient, but on the part of other members of the family in order to create the proper atmosphere and to afford

the necessary help to the patient. It is the duty of the physician to explain this fully to the friends and members of the family, so that they may cooperate thoroughly toward the one end, that of keeping the patient interested in his treatment, and avoiding distractions, worries, and excitements of various kinds. This is one of the hardest things to accomplish. It is far more difficult than furnishing open air sleeping apartments and it is no less important. The whole family must have confidence in the line of treatment and must be imbued with the necessity of aiding the patient to carry it out, otherwise failure is almost sure to result.

"The friends must know that tuberculosis is a chronic disease, which runs an uneven course. They must be prepared for the exacerbations of symptoms which come now and then, and must be able to encourage, rather than discourage, the patient at these times. It is necessary for the physician to tell them what their attitude toward the patient should be, and see that he obtains support and encouragement in carrying out his program. Friends must not be too solicitous. They must not nag. Nagging stirs up rebellion and destroys the spirit of cooperation. The patient must be treated as an intelligent being and must be expected to use judgment. If he does not, it is the physician who should correct him and not the attendants.

"I have seen many patients driven almost to distraction by over-anxious relatives and friends. Again, I have seen them throw away their chances of cure by following the advice of relatives and friends who tried to minimize the seriousness of their disease and urged them to do things which would prove harmful. Cooperation of all parties concerned is difficult to obtain, but indispensable to the highest degree of success. Whether this shall be obtained or not, will depend largely upon the physician.

"In the preparation of food for the patient care must be exercised. There is too much of a tendency on the part of solicitous mothers, wives, and others, to be too desirous of pleasing the fancies of the patient. The patient's appetite is not the proper guide to the food that he needs and should have. The friends who are around him, unless they are properly trained, have little, if any more, judgment than he; consequently it is the duty of the physician carefully to supervise the diet of the patient."

This is the age of specialization in medicine; but the really successful specialist is the one who realizes that his specialty is a part of internal medicine. It was necessary for specialists to take up the various departments of medicine and develop them, but it does not require a broad vision to see that their principal work is that of the pioneer. They are giving their thought and energy to some special subject that it may be developed and simplified in such a manner as to be utilized by general practitioners of medicine. Those who have added most to their chosen field of specialization, whether it be in the field of the eye, the nose and throat, diseases of the respiratory, circulatory, digestive, or nervous systems, cannot help chafing under the restraint of being specialists. They recognize that the symptoms which they are attempting to relieve are as apt to be, and in some instances more apt to be, dependent upon diseases of structures which do not come under their specialty than of those that do. They further are cognizant of the fact that the structures which are recognized as directly in their sphere of study cannot be considered apart from the other structures of the body. Medicine will be successful when it recognizes that the body is a unit, every part of which is affected by every other part, and that the whole is

dependent upon the normal action of every part; when it grasps the fact that a disease is of most consequence and is of the greatest interest to the patient as it affects him as a living, thinking, hoping being, and as it interferes with his productiveness.

I have made this seeming digression in order that my opinion of special institutions may be understood. Specialization in medicine requires specialization in institutional treatment, but if this is carried too far it is going to complicate rather than to unify medicine. There are some diseases which for various reasons should be treated apart; but these are few. What we must eventually aim at is efficiency and unity; and this will come when we have fully grasped the most important truth in clinical medicine,—that the pathological process, no matter what it is, must not be considered alone, but in relationship to the entire organism. In other words, clinical medicine must take into consideration the manner in which normal function is disturbed throughout the entire body.

From this it may be seen that the principles of therapy in all diseases must be much the same. Every system of the body must be taken into account. When our specialties have been fully worked out, not only as affecting certain organs and systems, but in their relationship to the important organs and systems which are not the seat of the primary disease, the unity of medicine will be a possibility and the internist be able to render efficient service in all ordinary diseases. When that time comes, it will be possible to successfully treat in general hospitals those diseases which are now being treated in special institutions; and the patient as an individual will profit by the change.

THE DIAGNOSIS AND THERAPY OF CHRONIC INTESTINAL TOXEMIA

BY GEORGE REESE SATTERLEE, M.D.,

NEW YORK.

Chronic intestinal toxemia is a term that has been loosely employed by many authors, but to those who are constantly studying intestinal conditions, it is a distinct entity and, although not a disease but rather a symptom complex of enteric pathology, it must be treated. Like uremia it is a complex; a poisoning of the system, originating in all probability from definite lesions of the gastrointestinal tract. It is often accompanied by pathological changes in the wall of the gut, usually localized to the right side of the colon. So far, the exact nature of the poison is no more proven than is that of uremia.

It is customary to speak of the toxemias of pregnancy and of nephritis as being of non-bacterial origin and of the toxemias of diphtheria, typhoid, pneumonia and other infectious diseases as being derived from the endo- or ecto-toxins or the end products of bacteria because we know that these diseases are of bacterial origin. The limitations of this paper prevent a detailed discussion of the different theories of chronic intestinal toxemia. The author however is strongly inclined to the view that it can be classed among the bacterial infections. A diseased intestinal mucosa and a metamorphosed colon bacillus capable of yielding a toxin are essential for this theory.[1]

The diagnosis of chronic intestinal toxemia is based upon three chief factors, the history, the *x*-ray, and the symptomatology and physical signs. The history of these patients begins frequently with an attack of acute indigestion and often a so-called ptomaine poisoning following the ingestion of some easily decomposed or indigestible article of food. This is followed by a prolonged interference with the digestive system and by nervous disturbances, the latter frequently predominating. The primary trouble is probably an intestinal putrefaction, the secondary a chronic intestinal toxemia in which the colon bacillus, metamorphosed, plays the important role due to the toxins liberated.

A brief description of the leading digestive symptoms is as follows:

Constipation.—Constipation may be congenital or acquired, usually the latter, but it frequently follows an abdominal operation. Occasionally a history of constipation is absent and the condition is discovered during radiography of the gastrointestinal tract; it is rarely absent but may be

replaced by diarrhea or colitis. In all probability, constipation, recognized or not, has been present and an important factor in the complaint. An alternation of constipation and diarrhea is quite frequent, constipation then being possibly the etiological factor. Evidences of this are the presence of fecal masses in the colon.

Flatulence.—This symptom is nearly always present and is evidenced by eructations and passage of flatus per anum. Abdominal distention may be present, with or without relief by the passage of gas but when marked and continuous is suggestive of intestinal obstruction. There may be considerable gas production with a soft and flat abdomen. Excess of gas bubble frequently remaining in one spot can be demonstrated in the radiographs. Abdominal pain is one of the results of distention of the gastrointestinal tract and the pain may be out of proportion to the amount of flatus. Kinks and adhesions may confine small amounts of gas and accentuate the pain but we must always consider the nervous susceptibility of the patient. A very common complaint is that "everything turns to gas."

Aerophagia is a frequent complication and can be sometimes demonstrated by fluoroscopy of the esophagus during deglutition. The patient frequently begins to belch and swallow gas immediately on entering the office although perfectly quiet while sitting in the waiting room. Palpitation of the heart results from distention of the cardia. It can be shown by fluoroscopy, the cardia gas bubble pressing up on the heart. A feeling of fullness after the ingestion of small quantities of a meal may be explained on these grounds, for when the gas bubble in the cardia is large it is difficult to make the patient swallow the whole meal. Dr. Aaron[2] finds bile in the stomach contents suggestive of this condition.

Flatulence due to abnormal fermentation or decomposition of carbohydrates may sometimes be distinguished from that caused by decomposition of proteins or putrefaction. The former is characterized by the lack of putrefactive odor to the gas expelled and the latter by the foul odor of the gases due to the formation of the putrescible substances, the phenols, indols, and other nitrogenous decomposition products of protein origin. Carbohydrate free diet will often clear up the former and a meatprotein free diet the latter, but very frequently the two kinds of gas formation are closely associated.

The Nervous System.—The mental symptoms are often far out of proportion to the extent of the lesion. Depression is marked and may even extend into a melancholia. The patient is extremely irritable and disturbed by small things that are usually passed by and the character is often completely changed. He is misunderstood by his family and immediate friends, although he appears normal to his acquaintances. There is lack of concentration and general inefficiency. These defects may lead to obsessions and even to dual personality. Attacks of vertigo, semi or complete unconsciousness, or convulsions resembling epilepsy are not infrequent. These

attacks can often be accompanied by or traced to an increase in the physical symptom of constipation, flatulence, and "indigestion." In the severest cases delirium, coma, illusions, or delusions may occur. The sensory, motor, and sympathetic systems are usually affected. Myalgias, neuralgias, and neuritides are very common and respond quickly to the proper treatment of the intestinal condition, resisting the usual coal-tar products. The motor symptoms are usually due to irritation to the central ganglia. Irritation of the sympathetic system is shown by vasomotor disturbances, as flushing of the face, tachy- or bradycardia, irritable stomach, dermatographia, polyuria, and interference with the ductless glands.

Joints.—Various forms of chronic arthritis are very common and possibly arthritis deformans. Joint pains and creaks with joint fremitus are very common.

Abdominal examination shows signs of intestinal stasis, crepitation over the colon, especially the cecum. Splashing, tenderness, and a "doughy" abdomen are very common. Signs of enteroptosis are contributing evidences of a tendency to this intestinal condition. They are positively to be looked upon as a frequent accompaniment of intestinal toxemia rather than as a direct cause. This point is of great importance in differential diagnosis as regards surgical intervention. Fecal masses in the colon can often be demonstrated and also collections in the rectum and sigmoid flexure.

Therapy of Chronic Intestinal Toxemia.—The treatment can be subdivided into that for (*a*) intestinal putrefaction and for (*b*) chronic intestinal toxemia proper.

The treatment of intestinal putrefaction consists of a primary purge, preferably castor oil, which should be given for two or three doses, one ounce every other day. The dietary is based upon the withdrawal of all meat protein or an admixture of carbohydrates and fats without complete protein withdrawal. This latter diet is given with the idea that if a sufficient quantity and quality of these substances be given they will withstand destruction and bacterial processes in the upper intestine (E. E. Smith[3]). The employment of this dietary may be very successful, but its efficacy may be shown by the use of glucose and starch enemata. The author believes in no compromise, however, and gives no meat protein for several days. Colon cleansing irrigations of saline solution are very useful here and should be given until all evidence of putrefaction are absent. Catharsis, fasting, and colon irrigations will usually clear up intestinal putrefaction. Fermented milk with lactic acid bacilli, buttermilk, or even sweet milk and cereals and simple stewed fruits alone should be given. Drugs at this stage are harmful. As putrefaction may occur at any stage of intestinal toxemia and often recurs, the treatment may have to be repeated.

Diet.—The diet in chronic intestinal toxemia proper is all important. (a) On account of the close association with and danger of intestinal putrefaction, it is necessary to withdraw all meat protein except that

contained in milk, cream, and butter. This includes all eggs, meat, fish, shellfish, and meat extracts. After a reasonable time, say three months, an egg and a little bacon is allowed and the patient watched for symptoms. Meat can then be added gradually if the grade of toxemia is a mild one. Relapses should always be treated by a complete withdrawal of meat.

(b) Prohibit all white refined flour and substitute whole wheat. The white flour of to-day is so highly refined that the nutritious substance (so-called "vitamines") and salts so necessary for proper metabolism have been removed. Prolonged eating of this white flour has shown bad results in intestinal toxemia, and it constipates. Polished rice should be placed in the same class and forbidden, non-polished and uncoated rice being substituted. If starch digestion is poor, it is unnecessary to eat large quantities of these two articles.

There are numerous difficulties in this dietary of whole wheat products to be overcome. I usually divide the patients into two classes: those who eat at home and those who eat in restaurants. Those in the former class have a much better chance than those who roam around for their meals. We often cannot spend much time on this class unless they will eat in certain specified restaurants where the dietary is cared for. Whole wheat flour does not keep well and is subject to parasites. It is not always easy to obtain. One reason of this is that it is not popular, as the public have not been educated as to its worth and it is not considered as palatable as the white flour. This can be overcome by the education of our cooks who can be taught to make delicious cakes, waffles, griddle cakes, biscuit, gravies, sauces, etc., with the whole wheat flour with but a small addition of white flour if necessary. If we should watch our cooks we would be amazed at the large quantities of white flour used in the preparation of our food.

Oatmeal and whole wheat cereals should be used freely; among the latter the old-fashioned cracked wheat is being revived and is an excellent substitute and a welcome change for the tired palate. The various proprietary and ready-prepared cereals are generally speaking poor foods, especially as all food should be properly cooked.

The modern corn products are also pernicious. Wood[4] says that they are low in nutritious substances, especially fats and phosphorus pentoxide, which is a reliable indicator of the so-called vitamine so essential to nutrition. In the place of these we should use the old-fashioned corn meal containing the sperm. Foods containing large amounts of finely milled flour should be classed as furnishing a "deficiency diet."

(c) Vegetables. Green vegetables are very important in the dietary. One factor in the improvement of our patients during the summer months, I believe, is the abundance of this class of food stuffs. Fresh vegetables are to be preferred to the canned, but cannot always

be obtained throughout the winter months except in the large cities where the small venders are of great value. I have tried in vain to get fresh vegetables in country towns during the winter and have had to ship them from the city. It is possible to obtain them if we take the trouble. Dried vegetables are excellent. The large hotels, however, feed their guests largely on canned goods for reasons best known to themselves.

I have had as patients head waiters in some of our best known hotels who inform me that they cannot obtain in the hotel restaurant the simple diet recommended. In certain instances the manager of the hotel has taken the trouble to place the diet within reach. The real reason of this condition is, of course, the lack of public interest and insufficient demand for the "simple life." In the choice of fruit vegetables, we must be guided by our idea of the condition of metabolism in the patient. A chemical blood analysis is necessary or at least of great help in determining the amount of sugar excess or retention. In cases of flatulent dyspepsia due to carbohydrate intolerance or where the blood sugar is above the normal limit, it may be necessary to restrict the vegetables to the class commonly designated as the 10 per cent. and 5 per cent. (carbohydrate) vegetables or in diabetes to the 5 per cent. vegetables alone. These are special cases where the diet has to be very carefully arranged.

Ordinarily the list of vegetables, all well cooked, includes string beans, young lima beans, spinach, asparagus, brussels sprouts, beet-tops, kale, rhubarb, celery and celery knobs, carrots, beets, squash, mushrooms, parsnips, turnips vegetable marrow, artichokes, cauliflower, and potatoes, white or sweet. Vegetable salads are useful to vary the monotony. They should be made with well cooked vegetables and lettuce, endive, etc., and dressed with olive oil and lemon juice in the place of vinegar, which may be a gastrointestinal irritant. Macaroni, spaghetti, and noodles, unless made from the whole wheat flour, are not permitted. In severe grades of intestinal toxemia the vegetable fats and oils should be substituted for the animal products as butter and cream, and are indicated when fats are needed for metabolism or for constipation.

(d) Fruit. Cooked fruit should be eaten at least twice and usually three times a day. Unless there is carbohydrate intolerance, the best fruits are apples, prunes, pears, and peaches, preferably fresh, but may be dried. Raisins, cherries, apricots, cranberries, huckleberries, blackberries, strawberries, raspberries, bananas—all cooked and preferably fresh—have their usefulness unless some idiosyncrasy exists. Of the uncooked fruit allowed are oranges, lemons, grapefruit, melons, unless some special reason exists for their being withheld. In glycosuric conditions, we must limit the fruit to the 5 per cent. or 10 per cent. (carbohydrate) fruit as indicated.

(e) Nuts are a welcome addition to the diet and are usually well

tolerated unless gastric digestion is very poor or some idiosyncrasy exists. They are walnuts, hickory nuts, pecans, Brazil nuts, peanuts, beech nuts, pine nuts, and almonds. These may be made up into bread, cakes, or desserts. They may be home ground in inexpensive mills which also grind wheat and corn. The 10 per cent. or 5 per cent. nuts should be carefully followed in glycosuric conditions.

(f) Milk Products. Milk is one of the most useful and often indispensable articles of diet. Sometimes it is contraindicated as when an idiosyncrasy exists or when it is constipating. Bacterial content has much to do with tolerance. Buttermilk or fermented milks will often counteract these effects. Sour milk or sour milk cheeses are very useful. The good effect of milk is probably through its lactose content as shown by recent experiments of Hull and Rettger[5]. Rennet is a very digestible and useful product. The cream cheeses are not so efficacious and the hard cheeses, such as American, Roquefort, Camembert, Swiss, and Dutch cheese, etc., are contraindicated on account of tendency to constipate. Cream is usually well borne and in 20 per cent. strength can be taken up to one-half pint per day; it is of aid in constipation.

Sugar is necessary and will make up for some of the calories lost by the reconstructed diet. Brown sugar or molasses helps constipation. Tea and coffee are allowed in moderation provided no contraindications exist. Cocoa or cereal coffee may have to be substituted.

In choosing vegetable foods it is interesting to consider those that have a high percentage of ash, the most important of which are phosphorus pentoxide, calcium oxide, and iron. According to the statistics of Henry C. Sherman[6], their order of value in percentage of edible portion is as follows: Rye and wheat bran, dried beans, cocoa, caraway seed, dried peas, almonds, peanuts, chocolate, oatmeal, rye flour, dried sweet corn, gooseberries, vanilla bean, and cottage cheese.

According to the percentage of 100 calories the following articles lead: Celery, canned vegetable soup, spinach, mushrooms, lettuce, leeks, pumpkin, rhubarb, asparagus, dried beans, cowpeas, string beans, turnips, parsnips, tomatoes, dried peas, fresh peas, cauliflower, and lima beans. The white potato is placed way down the scale chemically, but practical experience in Europe during the war has demonstrated that it is the most necessary of vegetable foods and cannot be wholly replaced by any other one vegetable. The potato should be baked or boiled in the skin, otherwise large amounts of the salts are lost in the water. This could be saved, however.

Among the foods, rich in carbohydrates, which should be avoided in marked flatulent dyspepsia, are in their order of carbohydrate content: corn starch, tapioca, hominy, rice, farina, oats, and prunes. Gelatin, being high in animal protein should not be used. Alcohol in any form is not to be used, as it is a gastrointestinal irritant.

Agar agar is in great favor with the author. Its use and method of

action by extracting water from the walls of the intestine and forming more liquid contents is well known. Its action is perfectly harmless and as a habit former is not bad. In some cases of colitis, however, it is irritating and causes pain and colic. It should be given in dram doses, mixed with the food three times daily; the dosage can be increased or diminished. It can be given in cracker or biscuit form and mixed with bran. It should not be medicated with laxative drugs.

Vaccine Treatment.—Autogenous colon vaccines are the most powerful agents that I know of in the treatment of chronic intestinal toxemia. Their rationale, preparation, and method of administration has been fully described by the author[7].

It is advisable to make an autogenous colon vaccine from the stool of every patient with a long standing intestinal toxemia. The results of administration are sometimes amazing and their least effect is to cure or improve the patient in about half the time usually taken by other means, if the case is suitable. The interval of dosage has been arbitrarily set at four days for six to eight doses, and then weekly. The severity of the case and the result usually determine their continuance and dosage. The initial dose is from 25 to 50 million and the maximum dose 300 million.

In relapses, which often take place, a few doses of the vaccine with a rigid diet will give quick results. In some cases, the author has accomplished results with the vaccines alone without a special diet, but he is convinced that the best results are accomplished in conjunction with diet.

It is essential to consider the liability to recurrences of intestinal putrefaction and right sided colitis already referred to as the usual lesion found to accompany chronic intestinal toxemia. Catharsis and irrigations should be used only at the discretion of the physician.

Drugs.—Drugs have very little effect upon these conditions except to be detrimental. Intestinal disinfectants, as phenyl-salicylate, creosote with lime, magnesium salicylate, castor oil in minimum doses, are sometimes of use, but we should always question the diet first and rule out some anatomical condition, such as ptosis or kinks or growths, before even thinking of them. Mineral oil is probably used more than any other form of therapy. In my own experience, it is only a makeshift but very useful where a proper control of the patient, as in dispensaries, is impossible. It may also be very useful when traveling, when some laxative is necessary and a proper diet unobtainable. Long continued ingestion of mineral oil will keep up intestinal toxemia because it does not cure the condition. The same objections or even stronger ones exist for olive oil which, however, if pure is excellent in small doses as a food and as a physiological cholagogue.

Colon Massage and Vibration.—In competent hands, mechanotherapy is not only very valuable but often essential. This method depends upon the skill and training of the attendant. A good colon masseur is part of the

office equipment. Real massage should take the place of all laxatives except as outlined by the diet. Electrical treatment of the abdominal muscles has given excellent results in the hands of many and is often indicated. It is not always easy to apply all this therapy to the busy man or woman, and often the financial means are limited. In many instances instruction will place the treatment in the hands of the patient so that with "medicine ball" abdominal exercises and the ordinary rules for constipation good results may be accomplished. These are, however, the simple cases in which the right colon is not seriously diseased.

Skillful vibration in the hands of the physician himself will often accomplish wonders and relieve in two to four weeks a constipation of over twenty years' duration. We notice the big drop in attendance in our intestinal clinic after a skilled colon masseur has left, for it is true that the poorer class of people generally know what is best for them and when they get results.

Enteroptosis.—Enteroptosis of moderate or severe grade should always be attended to. Posture is the keyword to this situation. Abdominal belts or preferably corsets are often essential. These must not only be mechanically efficient, but must also be applied under supervision of skilled attendants. The patients must be "followed up" and alterations made from time to time. A skilled corset maker and attendant are also part of the office equipment. Posture treatment should be carried on at night by the elevation of the bed. This can be done gradually, beginning with four inches in the very nervous and six in the others, raising by two inches every few nights until the limit of tolerance is reached, which is usually between twelve and eighteen inches.

The *psychological* side must not be lost sight of in therapeusis. One of the principal things that the patient needs is encouragement and suggestion that all will be well. It is often advisable to take the patient into your confidence and explain that relapses are the rule, but that they will be of short duration and less and less severe, and also that the improvement will be slow but progressive. If the doctor loses his patience and interest, the result in the patient is obvious. The real reason that many of these poor creatures do not get well is difficulty in obtaining the right sort of a doctor, who will persevere and be sympathetic but firm. It is a case of endless detail which does, we must confess, become monotonous. The fault lies often, however, on the patient's side, so that we can frequently foresee failure if we are good character readers. It is our duty, however, to give a fair trial in every case.

Surgical Therapeusis.—In every case where obstructive conditions such as adhesions, kinks, bands, intussusception, tumors, etc., exist, this is indicated. It is the border line cases that give us the most trouble. How is a decision to be reached whether or not a certain case should be operated on? What should be done after the abdomen is opened? At one time a

compromise operation called short-circuiting was very popular. The end results have been in the writer's experience, almost universally bad. Lane advised removal of the colon for every case of constipation that resisted medical treatment. This operation even in the hands of the expert has a high mortality and cannot be generally recommended. Draper has called attention to the functional importance of the left colon, experimentally, and he and Lynch have proved its value clinically. They have also shown why short-circuiting fails.

The so-called partial resection, or developmental reconstruction, of the colon to the second or primitive position, as practised by Bloodgood, Lynch and Draper, Mayo, and others, is a favorite with the writer in selected cases where the cecum and ascending colon are roentgenologically dysmorphic or so diseased as to resist medical treatment outlined above. It is not always possible to foresee the extent or character of the operation before laparotomy, but a persistent large residue of the opaque meal in the cecum with a profound toxemia, with no response to medical measures within a reasonable length of time, positively justifies operation. An operator experienced in this particular line is an absolute essential to success.

When the physical conditions are extremely bad and it is necessary to relieve the toxemia, ileostomy as rediscovered and popularized by Lynch (see Draper[8]) is very popular with the writer. This can be performed under local anesthesia and later a more radical operation done if advisable. The curative effect of simple ileostomy upon what Lynch[9] has called the segmental colitis of toxemia is often amazing. Appendicostomy and cecostomy give excellent results in special cases and can also be done with very little shock. The writer has seen several profoundly toxic and insane patients restored to normal mental equilibrium in this manner.

Plication of the enlarged bowel has given good temporary results, but has more often failed. It does not remove the cecocolonic focus of infection. Suspension of the colon and stomach in advanced and intractable ptosis is sometimes temporarily successful, but the author considers the basis for such operations as essentially faulty, physiologically, as is the short-circuiting technique. After all these operations it is necessary to consider that these are essentially medical cases and must be carefully followed up by medical treatment. In the author's practice medical and surgical therapeutics go hand in hand without any of the old discord and damaging jealousies. The author has seen a large number of operative cases, at first apparent failures, recover through energetic medical treatment.

Conclusions.—1. Chronic intestinal toxemia is a proper and useful term by which to describe a symptom complex which has its primary pathological seat in the cecocolon.

2. Position of the alimentary canal is etiologically important. The

carnivorous types of man are predisposed to toxemia. This may be due to other characteristics than mere morphology—which is an outward manifestation of unknown reactions to modern diet and conditions of life.

3. Since most symptoms are protective, constipation probably is. It is not the cause but an accompaniment of intestinal toxemia.

4. No case should be touched surgically until medical treatment, especially by colonic vaccines, has failed. In such cases it is probable that the cecocolon is extensively diseased and that no operation short of developmental reconstruction will be of permanent use.

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THE U. S. PHARMACOPŒIA, IX

BY HORATIO C. WOOD, JR., M.D.,

PHILADELPHIA.

Just one hundred years ago last January, Dr. Spalding submitted to the Medical Society of the County of New York, a project for the formation of a National Pharmacopœia, as the result of which proposition a general convention was held in Washington in 1820 and the first U. S. P. was published in that year. This work was merely a list of the drugs which were deemed of sufficient importance, with directions for the manufacture of certain preparations made from them, and was the work solely of physicians. In 1840 the cooperation of colleges of pharmacy was requested and since then the apothecaries' share in the revision of the work has become so important that one often hears physicians declaiming that the Pharmacopœia is of no use to the doctor. Such a statement always makes me suspect that the speaker does not possess a copy of the Pharmacopœia and has never carefully perused it. While in modern commercial conditions the doctor is not directly interested in the details of methods of assay and tests of identity and purity, there is much matter in the Pharmacopœia with which he is immediately concerned. For myself I can only say that the Pharmacopœia is one of the most frequently consulted books of reference and always, I believe, with advantage to my patients.

To the up-to-date physician the appearance of a new revision of our national standard is an event of real importance. I am glad, therefore, of an opportunity to say a few words of some of the more striking changes in the latest edition which is deserving of commendation for its virtues both of omission and commission.

Let me briefly speak first of the things which have been left out. Most important among these are a lot of worthless herbs such as camomile, bone-set, horehound, burdock, cypripedium, scutellaria, sage, pennyroyal, marigold, and other similar truck which has littered up our national standard for many years. There are a few of this class of drugs still retained as a sop to the superstition of a diminishing number of practitioners. While I shall be glad to see the last of them I am gratified to see that the present revision committee has succeeded in evicting so large a number.

Similarly pleasing, especially to those of us who have had to teach materia medica, is the fact that nine salts of iron have been dismissed. One could not say that these were worthless for they possess the thera-

peutic virtue of iron in general, but they were certainly quite needless as we still have ten preparations of this metal available. If perchance any of you have lost a pet form of iron you can find it by applying to the National Formulary.

An omission about which there has raged, and still is raging, an acrimonious discussion is that of the alcoholic beverages, wine and whiskey. Personally, I am convinced that, under certain circumstances, alcohol is a valuable therapeutic remedy but my belief in the medicinal usefulness of alcohol does not necessarily imply the necessity of a Pharmacopœial standard for whiskey. There were strong arguments brought forward in the discussion of this question in the committee on revision by both sides, but I think the reasons which finally resulted in its deletion were, first the divergence of opinion as to the reliability of certain tests for differentiating artificial from natural whiskey; secondly the fact that the U. S. Government has a standard for labeling whiskies and their imitations independent of that of the Pharmacopœia, and that if the Pharmacopœial standard differed from that of the Department of Agriculture it would be commercially unenforceable. I was much struck by the remarks of Dr. Osborne in this connection, who said that if we wanted to obtain the therapeutic action of alcohol and stick to pharmacopœial preparations, we had such a whole host of available substitutes in such mixtures as tincture of gentian, compound tincture of cardamon, aromatic elixir, etc. We are sometimes prone to forget that we can obtain all the action of alcohol by administering alcohol. It is not necessary to drink whiskey to become intoxicated.

More interesting than the deletions, however, are the innovations. Perhaps the most important of these is the official recognition—for the first time, I believe, in the history of the world, certainly in the history of this country—of physiological standards for such drugs as digitalis, cannabis indica, hypophysis, and suprarenal. In cases of aconite, digitalis, strophanthus, squill, and suprarenal the biological standard is advised, but is made compulsory only in the cases of cannabis and solution of hypophysis. Some may question what is the advantage of a standard which is not compulsory. The advantage lies in the fact that manufacturers can no longer advertise their compounds as biologically assayed unless they conform to the Pharmacopœial requirements as to potency. Hitherto certain manufacturers have put upon the market preparations of digitalis or other drugs which were claimed to be physiologically standardized but the standard for whose activity was any indefinite degree of potency that happened to suit their whims. Now a preparation which is physiologically standardized must conform to the requirements of the Pharmacopœia.

Among the newer synthetics which have won for themselves an important place in our armamentarium several have achieved official rec-

ognition, although, regrettably, some have been omitted through fear of legal complications on account of protecting patents. Of those which have been admitted I may mention first two morphine derivatives, ethyl-morphine, and diacetyl-morphine. Let me beg of you to forget the trademark names for these two popular and valuable drugs. Of the value of these drugs and the range of their usefulness it is hardly necessary for me to speak. I might, however, point out that they differ considerably from each other and from their common ancestor morphine. The diacetyl-morphine is, both relatively and absolutely, much more actively depressant to the respiratory center than is morphine. Because of its absolutely greater power it must be given in much smaller dose and because of its relatively greater sedative effect upon respiration it is of much less value as an analgesic than morphine. In cases where an effect upon respiratory function is desired, as in excessive cough, or especially in bronchial asthma, I think the diacetyl ester is generally to be preferred to morphine as being not only more certain but, in the doses required, less disturbing to the alimentary canal. Ethyl-morphine, on the other hand, is distinctly less active than morphine and more closely resembles codeine, which is a methyl-morphine, than it does the mother alkaloid. In my own experience it has seemed to possess greater anodyne properties than either codeine or acetyl-morphine, although of course greatly inferior to morphine. It has the very great advantage, however, that there is much less danger of habit formation from its use; in fact I have never heard of a case of habit from either ethyl-morphine or codeine.

A much less widely known novelty is sodium perborate. This super-oxygenated compound in aqueous solution yields up an atom of oxygen which unites with the elements of water to form hydrogen dioxide, and leaving behind the alkaline sodium pyroborate, not the sodium borate of the Pharmacopœia, commonly called borax. Because of the alkalinity of the solution formed by the hydrogen dioxide is rapidly decomposed with the evolution of oxygen. This salt offers a means of preparing extemporaneous solutions of peroxide of hydrogen. Seventy grains of sodium perborate to an ounce of water gives a solution about equivalent in anti-bacterial properties to the official solution of hydrogen dioxide; for convenience of remembering we may say to use from one-half to one drachm per ounce. The solution must be freshly prepared immediately before use.

Solomon is supposed to have remarked that there was nothing new under the sun, and the present fashion in laxatives is an illustration of his perspicacity. Some thirty years ago Dr. Randolph of Philadelphia recommended the use of petrolatum in the treatment of chronic constipation. He had quite a number of followers in this use and for a short time the drug enjoyed considerable popularity, and then we all forgot

about it until Sir Arbuthnot Lane introduced the use of the liquid petrolatum, or as it is popularly called, mineral oil, for the same purpose. The effects of petrolatum, whether in the liquid or semisolid state, are essentially identical. Namely, it gives a soft, indigestible, but inoffensive material to lend bulk to the passages and perhaps may have some lubricating effect. There is a common belief that the more viscid mineral oils are less prone to ooze out through the sphincter ani, and the Pharmacopœia has therefore recognized two forms of liquid petrolatum, a light one intended for use in atomizers, and heavy viscid oil for internal use. If there be any truth in this idea that the more viscid oils are to be preferred for this purpose it would seem rational to go back to Dr. Randolph's custom and use the semisolid rather than the liquid petrolatum.

Incidentally it is interesting to note how fashions in laxatives, as in clothes, change for no apparent reason except the whims of the medical public. When the committee on revision began its work agar-agar was enjoying its brief period of reclame as the *ne plus ultra* for the mitigation of sluggish colons, just as to-day does liquid petrolatum. This cellulose-like extract of Japanese sea weeds acts because, like petrolatum, it is entirely unaffected by the digestive juices and passes through the intestinal tract unabsorbed. By virtue of its own bulk, but especially because of its power of holding water, it gives mass to the contents of the colon. So fleeting are fashions, however, that this drug, which was in the zenith of its popularity at the beginning of the work of revision, had almost passed from notice before the Pharmacopœia appeared. While speaking on the subject of laxatives I may call your attention to the fact that phenolphthalein, which had long been considered in the appendix of the Pharmacopœia only as a test for alkalies, has now been moved to the body of the book because of its popularity as a cathartic.

A very interesting addition is phenylcinchonic acid which was introduced some years ago as the result of the studies of Nicolaier. He found that the administration of this agent greatly increased the amount of uric acid in the urine—sometimes as much as 200 or 300 per cent.—without a corresponding increase in the other nitrogenous bodies. This fact has been abundantly confirmed and holds true in both gouty and normal men and for all sorts of diets. The theory which has been advanced that the increase in the output of uric acid was due to an increased formation of this substance in the body is no longer tenable because the observations of Folin and Lyman have shown that there is accompanying the increased output a diminution in the amount of uric acid in the blood. We must concede, therefore, that the drug in some way raises the permeability of the kidney for uric acid. Because of this effect it was argued that it would prove a useful remedy in gout.

The chain of reasoning is weak, however, in one link, namely that at present we have no definite knowledge of the relation between gout and uric acid, although the disease seems in some way to be associated with disturbances of purin metabolism. Nevertheless there is a certain amount of clinical testimony of the value of the drug in gouty conditions. Phenylcinchonic acid appears also to possess some analgesic powers apart from its influence upon uric acid secretion and has been used in other forms of arthritis.

Another substance originally introduced as a proprietary, which has received official recognition, is cotarnine, of which the hydrochloride is official. This alkaloid, which is manufactured from narcotin, has been used under the trade names of stypticin and of styptol. Its most important physiological action is a stimulating influence upon the unstriped muscles, especially of the uterus. By virtue of this effect it is a valuable remedy in various forms of uterine hemorrhage. Just as in the case of ergot, the effect of cotarnine in uterine bleeding has led to its employment in other forms of internal hemorrhages. There is, however, no rational explanation of any styptic action and in the absence of any scientific reason I am constrained to be skeptical of its real value in these conditions, despite a considerable number of clinical reports which are apparently favorable.

Among the drugs of non-proprietary character which have won their way into the Pharmacopœia I might mention sodium cacodylate, calcium and sodium glycerophosphates, emetine hydrochloride, quinine and urea hydrochloride, and trinitrophenol. The cacodylates were so clearly and conclusively presented to this society some years ago by Dr. Dawes that it does not seem necessary to say anything more about them, except to warn against their administration by mouth which frequently gives rise to an almost unendurable garlicky taste and odor.

The question of the effects of the glycerophosphates upon bodily nutrition, especially of the nervous system, is as yet *sub judice*. The experiments bearing on its utilization by the tissues have been so extraordinarily contradictory that it is impossible to draw final conclusions. The mass of evidence, however, seems to me to strongly indicate that they are little, if at all, more easily metabolized than the inorganic phosphates. But even if it were finally determined that the glycerophosphates were of no value from the nutritive standpoint that does not necessarily preclude their therapeutic usefulness. It is pretty well established that elemental phosphorus stimulates the growth of bone, but in view of the infinitesimal doses employed it is absurd to imagine that it supplies the needed element for the synthesis of bony tissue. Its action is much more rationally attributed to some stimulating influence upon anabolism of the same nature as that caused by arsenic or

quinine or various other drugs. While not as yet demonstrated it is not unreasonable to consider the possibility that the glycerophosphates may exercise a similar stimulant effect upon the vital chemistry.

Trinitrophenol, more familiarly known as picric acid, has for many years been highly esteemed by a small group of surgeons, especially in the treatment of burns. The recent investigations of Schamberg and Kolmer have established that it is a very much more potent germicide than carbolic acid; they give its phenol coefficient as between 4 and 5. It differs from phenol in being actively astringent as well as germicidal. It is likely to become of increasing importance in certain skin diseases as well as in burns and other open ulcers. It has two disadvantages which militate against its greater popularity, first its powerful staining properties and secondly the occasional occurrence of dermatitis from its use. A most extraordinary dermatitis occurs among the workers in munition factories who have come in contact with picric acid.

As there have been nearly forty drugs, not including new preparations, which have received official recognition for the first time it is manifestly impossible to consider them all in detail.

Besides those already considered may be mentioned betaeucaine hydrochloride, creosote carbonate, bismuth betnaphtholate, quinine and urea hydrochloride, emetine hydrochloride, and a number of others. An entirely new departure has been made in the recognition of compressed gases, of which nitrogen monoxide and oxygen have been admitted.

Of the new pharmaceuticals attention may be called in the first place to the powdered extracts, which are for the first time official. The majority of the extracts of the U. S. P. IX are now in the form of powder, although cannabis, indica, ergot, hyocyamus, sumbul, gentian, and one or two others less important are still directed to be of pillular consistence. Among the extracts is found the Extractum fellis bovis which replaces the old purified ox-gall. This extract of ox-gall is practically the same as the compound commonly called sodium cholate and is practically a mixture of the glycocholate and taurocholate with small quantities of organic impurities plus the addition of sufficient starch to make one part represent eight parts of ox-gall.

Another interesting type of pharmaceuticals are the magmæ of which two have been admitted, Magma bismuthi, or milk of bismuth, and Magna magnesiæ, or milk of magnesia. These are suspensions respectively of bismuth and magnesium hydroxides without the intervention of any mucilaginous vehicle, and offer a convenient way of administering these drugs. One fluidrachm of the milk of bismuth corresponds approximately to 4½ grains of bismuth subnitrate. Each

fluidrachm of the milk of magnesia represents about 3 grains of magnesium oxide.

A novel departure of great interest to the physician is an article in the appendix on the diagnostical reagents and clinical tests. This includes formulæ for the preparation of various solutions used in the clinical examination of urine, of blood, gastric contents, and sputum, as well as directions for the preparation of the various culture media and stains frequently used in bacteriology. If you have ever wanted to have a druggist make up a small quantity of Toisson's solution in a hurry or wanted to know the proportion of citric acid in Esbach's reagent, you will not have to be shown the practical utility of this collection of formulæ.

I have trespassed already too much on your patience although I have only touched on some of the more salient features of the Ninth Revision of the United States Pharmacopœia. In conclusion I would say to you, Get a copy and study it and you too will become boosters.

A CRITICAL ANALYSIS OF THE TREATMENT OF TUBERCULOSIS WITH COPPER AND POTASSIUM CYANIDE

BY GEORGE H. EVANS, M.D.,

SAN FRANCISCO, CAL.

Assistant Professor of Clinical Medicine, University of California Medical School.

The brilliant achievements of Ehrlich in the chemotherapy of syphilis have anew called the attention of the medical profession to the possibility of the discovery of a specific for tuberculosis among the metallic substances used in medicine. Attention for the meantime has been to a certain extent diverted from biologic remedies by the impetus given by the researches of Meissen, von Linden, Dewitt, Koga, and others in the field of chemotherapy. In these studies, gold, copper, arsenic, iodine, and other substances have had their respective advocates, and results of animal experimentation and clinical experience have been presented, sometimes with an enthusiasm which would almost suggest that the great panacea for tuberculosis was in our hands. A critical analysis, however, usually demonstrates that the optimism of the therapist has been responsible for deductions not in accordance with the actual results, and thus remedy after remedy is brought forth only to be consigned to therapeutic oblivion.

A curious misapprehension popularly exists in the mind of the public, and to a certain extent in that of the profession, that a specific remedy for tuberculosis is possible in the sense that such specifics exist for malaria, diphtheria, or even syphilis. This is due to the popular misapprehension concerning the pathology underlying chronic phthisis in the adult, the result and development of tuberculosis which has existed since early childhood.

Thus we see these remedies presented and advocated as specifics, based on the result of animal experimentation. It is quite a different thing to inhibit or even heal a recent tuberculous lesion experimentally produced, from successfully attacking bacilli firmly intrenched behind impenetrable barriers of fibrous tissue, the result of years of development. We read much in literature concerning the curability of early tuberculosis. It is time we changed our views in accordance with the facts brought out by modern studies of phthisiogenesis, and recognized the fact that incipient pulmonary tuberculosis in the adult does not exist; that phthisis is a pathological process, the result of years of tuberculous disease, where, in the favorable cases, processes of destruction and repair have gone on hand in hand. The lessons of the autopsy table surely teach this.

Last year Koga, working in the Kitasato Institute for Infectious Diseases in Tokyo, presented two contributions to the chemotherapy of tuberculosis. After considerable experimentation with different substances and different solutions of the same substances, he prepared a double salt of copper and potassium cyanide, put up in dilution of two milligrams of the salt to the cubic centimeter of diluent. The results recorded by him were such as to justify a careful clinical trial of the merits of the preparation. Through the kindness of Dr. Koga a sufficient amount of the remedy for study was placed at my disposal, and the following case records are from my wards in the tuberculosis department of the San Francisco General Hospital.

The criticism will at once be made that an insufficient number of patients has been studied on which to base any conclusions as to the value of the remedy. Such criticism must be met by the statement that a critical analysis of a few cases intensively studied and carefully observed affords a better basis for subsequent study than does a large clinical material where the facilities are frequently not such as to allow of such intensive study and observation.

Out of a service of about seventy beds, ten patients were selected for treatment. The service in this department is for the reception of late cases only, and the preparation therefore was put to a rather severe test. On the other hand, the favorable results usually accomplished by dietetic-hygienic treatment on the earlier cases generally renders any conclusion impossible as to the value of this or that remedy which may have been tried.

The cases selected presented a variety of tuberculous lesions and complications and were chosen without much regard to their severity, in the attempt to determine better the immediate effect of the preparation upon tuberculous tissue generally.

In the examination of these patients, careful records and studies were made of the blood, urine, functional kidney tests, amount and content of sputum, etc., and other chronic conditions were ruled out as far as possible. With one exception the Wassermann blood-serum test was negative. Tubercle bacilli were present in the sputum of all.

The preparation was used in doses varying from eight to twenty-one milligrams, and was invariably given intravenously, a vein in the elbow being chosen. Scarcely any difficulty was experienced in the administration. Occasionally some soreness and temporary induration were experienced by a few drops of the material getting into the perivascular tissues. The patients were confined to bed during the first week following each injection, some of them during the entire course of the treatment. Those who were allowed up were strictly limited as to their activity.

It was administered at intervals of two weeks following the plan of Dr. Koga.

Case I.—Walter P., age 29, a waiter, born in the United States, entered the San Francisco Hospital December 6, 1916, complaining of cough, weakness, loss of weight and pain in the left chest. He had a cough eighteen years ago, and was told then that he had tuberculosis. He apparently recovered and enlisted in the army. He had had several attacks of tonsilitis, and a fistula in ano was operated upon last May. His present illness had begun two years before with a severe cold. He lost weight, became weaker and had night sweats. His weight on entrance was 142 pounds, representing a loss of 46 pounds. He had used alcohol to excess, denied Neisser or luetic infection, had chancroid when in the Army.

Examination showed a man somewhat emaciated, with dullness over both upper lobes, rales in the right upper lobe, and signs of cavity in both apices. His urine was negative, with a total phenolphthalein output of 58 per cent. Blood examination was negative. Wassermann blood serum test negative. Tubercle bacilli were present in the sputum, Gaffky 1.

Treatment: On January 14, 1917, 8 mg. of the copper and potassium cyanide was administered intravenously; it was almost immediately followed by a chill of 10 minutes' duration. The following day showed a rather prompt rise in temperature and pulse, soreness in the chest, with slight increase in rales. There was some soreness around the scar of the old fistula in ano, which appeared inflamed. On January 28, two weeks later, 12 mg. were injected, followed by slight dizziness. The next day there was again soreness in the chest. The sputum, however, had decreased, the cough was less, and no bacilli were found. On February 12, 12 mg. No general reaction followed this, but the next day there was some increase in sputum and pain in the chest. There was some local pain in the arm for some time following this injection. February 26, 16 mg. were given, followed by considerable perivascular infiltration and some increase in the sputum, which was blood streaked. March 12, 17 mg. was given without reaction. March 29, 12 mg. was injected. The next day showed a slight increase in the number of bacilli, but no general reaction.

This man's weight increased from 136 pounds to 145 pounds during the treatment. While his general condition seemed considerably improved, there was very little change in the physical signs, and bacilli were still present.

Case II.—Chris. F., a student, 21 years of age, born in the Philippine Islands, entered the San Francisco Hospital November 16, 1916, complaining of cough, hoarseness, weakness, and night sweats. He had lived for the past four years in San Francisco. The only history of significance was an attack of smallpox when four years of age. He denied symptoms of his present illness before September, 1916, at which time he began to have a slight morning cough and pain in the chest; later hoarseness developed, which had increased; in October night sweats appeared. His weight on entrance was 109 pounds.

Examination showed a fairly well developed and nourished young man, well pock-marked, with bad tonsils and poor oral hygiene. The larynx showed ulcerations on the right cord. The chest was normal in shape, with considerable regional emaciation and extensive tuberculous involvement of both lungs, more marked on the left, and cavity formation in the left upper lobe. The heart was small. Blood pressure 138, 98. Urine negative with a phenolphthalein output of 45 per cent. Blood and Wassermann negative. Tubercle bacilli in the sputum.

Treatment: On January 15, 1917, 8 mg. of the double salt was given, followed by a chill lasting 15 minutes. The next day there was focal reaction shown by slight increase in the sputum and some pain in the throat. On January 29, 15 mg. was given, followed the next day by a slight increase in sputum. On February 12, 8 mg. This was not followed by any reaction. February 26, 12 mg.; no reaction except

some local induration at the site of the injection. He stated that his throat was considerably better. On March 4, six days after the last injection, he developed a sudden pain in the chest, with sharp rise of temperature to 104°. A spontaneous pneumothorax had occurred on the left side. This was accompanied by painful respiration, increased pulse, and slight increase in the sputum. The next day the sputum had markedly decreased. On March 13 fluid was present in the left pleura in considerable quantity. Thoracentesis (5 c.c. withdrawn) showed a clear transudate; 14 mg. of the cyanide salt was given, with no evidence of reaction. The temperature remained high. On March 26 the pleural fluid was decreasing in quantity. On April 26 his hoarseness continued, the pleural fluid had apparently been entirely absorbed, and the temperature had been nearly normal for three weeks. Sputum was present in negligible quantities. His weight, which was 105½ pounds at the beginning of treatment, decreased during the attack of pneumothorax, but increased again to 103¼ pounds.

There was very little change in the condition of the lungs except that produced by the changes in the pleura. There was no demonstrable fluid remaining. The larynx had not improved. This man was very optimistic and thought he was better, but the prognosis is bad. He still had bacilli in his sputum, Gaffky 2.

Case III.—Karl S., age 31, single, cook, born in the United States, entered the San Francisco Hospital on December 18, 1916, complaining of cough and shortness of breath, which had existed for seven months. He had had night sweats for six months, and a week before there had been blood in his sputum. He had been subject to frequent colds for the past twenty years. Admitted Neisser infection; denied lues. Had formerly used alcohol excessively. Lately his appetite and digestion had been disturbed and there had been considerable dyspnea. Temperature on entrance was 100°, pulse 85.

Examination showed both lungs involved in an extensive tuberculous process, with cavity formation at the left apex. The *x*-ray plate showed considerable mottling throughout the right lung, with dense fibrous shadow in the left upper lobe. The heart was ptosed. The bases were fairly clear, the left emphysematous, the diaphragmatic domes well marked. The sputum contained tubercle bacilli, Gaffky 3. Urine and blood were negative, except that the Wassermann in this instance was ++. (This was the only case in the series presenting a positive Wassermann.)

Treatment: January 16, 1917, 8 mg. of the double salt was given, followed by a slight chill and some headache. January 29, the man's general condition was much improved—rales had diminished and there was less cough; 16 mg. was administered, followed that night and the next day by pain in both sides of the chest, some increase in rales on both sides, and increase in sputum. Two days later there was a decided increase in his leucocytes. On February 12 there were very few rales present—decidedly decreased in number in both apices; 12 mg. administered. This was followed by slight pain at the site of injection. There was no focal or general reaction. Sputum had disappeared. On February 16 he felt well and wanted to leave the hospital, which he later did without permission.

This man's weight increased from 133 pounds to 142½ pounds. His sputum, which was quite abundant at the beginning of the treatment, steadily decreased, and after the increase marking the reaction from the second injection, entirely and permanently disappeared.

Case IV.—Gustav P., age 59, single, a Russian sailor, entered the San Francisco Hospital December 4, 1916, complaining of cough, much sputum, dyspnea, loss of weight, and recent hemoptosis. His father died of tuberculosis. Patient had at times been immoderate with alcohol; denied venery. His present trouble began

about four years ago with a cough which had gradually increased. Occasional fever, night sweats, and chest pains on the left side. During past two years had lost 20 pounds in weight. For past year he had had nausea and vomiting, with weakness, cough, and dyspnea.

Examination showed a man fairly well developed, without marked emaciation. Fingers clubbed. He had an emphysematous chest with considerable muscle atrophy in the clavicular fossæ, with dullness over the upper lobes and hyperresonance below. He had excessive crepitation through both lungs, with marked asthmatic rales on both sides. There was cavity formation in the left upper lobe. Examination of the heart was negative. Blood pressure 105, 70. Urine was negative. Phenolphthalein function 53 per cent. Blood count and Wassermann negative. Sputum contained tubercle bacilli, Gaffky 3. Tuberculin reactions were mild and delayed, both cutaneous and intracutaneous. X-ray plate of his chest showed extensive mottling throughout both lungs, with much fibrosis in the apices.

Treatment: 12 mg. of the copper and potassium cyanide was given on January 18, 1917, followed by an increase in the number of rales, some chest pain and traces of blood in the sputum. No general reaction. On February 1, the second dose, 16 mg., was given. Following this there was some increase in the number of leucocytes, the sputum became thicker and a few blood clots appeared on the second day February 15, 14 mg. The next day there was slight pain in the chest and the sputum had somewhat increased. There was also some local tenderness at the site of injection. March 1, 16 mg. was given, with evidence of focal reaction, the rales again being increased, with some increase in the bacillary content of the sputum. During this time, and since his entrance, he had been continuously vomiting in the morning, with considerable burning sensation in his stomach; this had been relieved by alkalis. March 15, 13 mg., without any evidence of reaction.

This man's weight increased from 137 pounds to 145 pounds. His physical signs had improved somewhat, although the bacillary content remained about the same. There had been very little change in the actual amount of sputum compared with the beginning of treatment. Traces of blood were frequent during treatment, but with very little relation to the time of injection. The man was of the emphysematous, fibroid type, essentially chronic, where one frequently sees periods of remission regardless of any treatment. His mental attitude toward his disease was, of course, very much improved.

Case V.—Bernard O., Italian laborer, age 27, entered the San Francisco Hospital December 28, 1916, without a very satisfactory history. As far as it could be obtained, his disease had begun 3½ months before, with cough, sputum, night sweats and hemoptysis. He had dissipated considerably and his weight had decreased from 140 pounds to 106 pounds. He had been steadily failing since his entrance to the hospital and had been running a high septic temperature with correspondingly rapid pulse.

Examination of the chest showed extensive bilateral disease with probable cavity formation in both apices. There was, in addition, considerable laryngeal ulceration and he was coughing large amounts of sputum, Gaffky 7.

The prognosis was considered hopeless in this case. He gained somewhat in weight during his stay in the hospital, and at the time treatment was commenced had increased to 119 pounds, but temperature and pulse were still running very high.

Treatment: Three injections of the double salt were given, of 6, 7 and 10 mg. respectively, at intervals of two weeks. Aside from a chill lasting 20 minutes following the first injection, no symptoms referable to the injection could be determined. He lost steadily and died 40 days following the first injection. His temperature,

pulse, sputum, and throat symptoms remained unchanged during this time. Autopsy showed extensive tuberculous involvement of both lungs, with large cavity formation. There was no evidence of tuberculosis in any of the other organs.

Case VI.—Henry B., a Swiss laborer, age 48, single, entered the San Francisco Hospital November 13, 1916, complaining of cough, weakness and loss of weight. He denied venery, had always been moderate in his habits, and had always been well and strong until six years before, when he sustained a compound fracture of the leg. During the following 16 months he had lost in strength and weight and suffered from malaise. Six months before entrance he had severe pleural pains in the left side of the chest, followed shortly by a brisk hemorrhage. Cough had persisted and steadily increased. He had a second hemorrhage one month after the first, and since has had occasional night sweats and intermittent attacks of fever. Recently coughing had produced vomiting. No intestinal disturbance.

Examination showed a poorly developed and nourished man, markedly emaciated. There was an extensive tuberculous process involving both lungs, more marked on the left, with cavity formation in the left upper lobe. The heart was displaced somewhat to the left, apparently the result of adhesions. His abdomen showed his liver somewhat enlarged and tender, the spleen was palpable, and there was considerable tympanites. Tuberculin reactions, cutaneous and intracutaneous, were delayed and mild. Blood pressure 115, 75. Urine, chemical, microscopical and functional, negative. Blood and Wassermann negative. Sputum contained tubercle bacilli, Gaffky 3.

Treatment: January 23, 1917, copper and potassium cyanide, 12 mg., followed the next day by headache and some increase in rales. February 6, the sputum had very much decreased in quantity since the first injection, being less than one-third the amount; an injection of 16 mg. was given. This was followed the next day by a temporary increase in sputum and bacillary content (Gaffky 1-3). There was no evidence of general reaction, but he complained of some pain in the region of the left shoulder, which he admitted had been present since the first injection. He had a restless night because of some perivascular infiltration at the site of injection. February 20, 21 mg. given. Seven hours following this rather large dose, he complained of malaise, with occasional sharp pain in the left chest. The next day there was a slight rise in temperature (100.6°), some rise in pulse, and a slight increase in leucocytes. The sputum was also increased. The temperature remained up for four days following the injection. The leucocytes were up for two days, when they fell to normal. During these days he was nervous, slept poorly, had general aching sensations, felt tired, appetite poor, and he had slight chills for two days. There was a feeling of oppression in the chest and an increase of the sputum for four days. His cough had increased; he required heroin for his relief, and there was general depression. On March 1 he felt better, though the cough was still troublesome and there were occasional traces of blood in the sputum. March 6, 13 mg. was administered, followed by some increase in rales, sputum and bacilli. No general reaction. He felt much better than usual and his appetite had improved. March 22, 13 mg., without any evidence of reaction, local or focal. He felt very well and was anxious to be up.

On April 26, examination of the chest showed practically unaltered physical signs. During the treatment his sputum had been reduced to practically negligible quantities. His weight increased from 113¾ pounds to 121½ pounds. His general condition, physical and mental, was very good, and he was exceedingly optimistic. The reactions following the third injection were probably due to the large dose.

Case VII.—Eva H., age 29, widow, entered the San Francisco Hospital November 1, 1916, complaining of cough, loss of weight, night sweats, vomiting, hoarse-

ness, and occasional hemoptysis. She had been troubled with bronchitis for the past five years and had coughed constantly since February, 1915, with hoarseness. Said she had been run down for the past four or five years, and had had night sweats for the past year. Since August, 1915, she had had frequent hemorrhages, two of them severe. She was about 15 pounds below her usual weight.

Examination showed a poorly nourished, anemic woman, with excessive cough, emaciated, with extensive bilateral disease, more marked on the left, where the entire lung was involved in a tuberculous process with considerable destruction in the apex. Rales were heard throughout. There was dullness throughout the right upper lobe, with rales at the apex and probable small cavity under the clavicle. The *x*-ray plate showed practically the same extent of disease. The urine, blood, and Wasserman were negative. Temperature was running between 100° and 102°, with very rapid pulse. The prognosis was extremely bad.

Treatment: Treatment begun January 26, 1917, when 12 mg. were given. This was followed by the most severe focal reaction of the series. The next day her hoarseness had increased and there was complete aphonia. Examination of the larynx showed the arytenoids so swollen that a view of the interior of the larynx could not be obtained. The sputum had increased, the cough was very troublesome, and there were extensive sticky and moist rales throughout the left lung. These evidences of focal reaction remained for about 10 days. There was no general reaction. February 9. During the past week she had had an attack of tonsillitis. An injection of 10 mg. was followed the next day by slight focal reaction and some soreness at the site of injection. February 23, 12 mg., with slight focal reaction, as shown by some increase in sputum. Cough still troublesome. March 9. Night sweats had been frequent and severe during the previous week; 10 mg. given, with increase in sputum and cough appearing two days after the injection.

This woman's weight decreased from 104 pounds to 98 pounds during the treatment. She became steadily worse, but had been losing ground before. She had been febrile throughout, but during the latter part of the treatment the temperature became higher with more extensive septic swings. On May 1 she was too weak for thorough examination of the chest, but showed that the disease had been progressing. It is possible that she was made worse by this treatment (note the severe focal reaction following the first injection).

Case VIII.—Minna B., widow, age 25, entered the San Francisco Hospital May 3, 1916. Two weeks before entrance she had had severe hemoptysis, since which time she had had cough and pain in the left side of the chest. She had lost 10 pounds in weight. She remained in the hospital for five months under dietetic-hygienic treatment, when she was discharged very much improved. Bacilli had disappeared. She was readmitted January 18, 1917, having had several brisk hemorrhages during the preceding two months.

Examination on readmission showed activity on the left side from the apex to the angle of the scapula, with dullness and some rales over the right upper lobe. The *x*-ray plate showed an extensive process throughout the left lung, with the heart shadow shifted to the left—the result of fibrosis. The left lung shadow was particularly dense in the lower part. There was some mottling on the right side, with a few discreet gland shadows. She had a temperature of 100° and pulse of 100. The urine and blood were negative. Blood pressure 120, 83. Tubercle bacilli were present in the sputum, Gaffky 1.

Treatment: On January 26, an injection of 12 mg. was given, followed the next day by slight pain in the chest, but no general reaction or change in the physical signs. January 9, 16 mg. given, followed in two hours by sharp pleural pain

in the right side of the chest. The next day there was a definite increase in rales, some of them being moist. Rales were also heard in the right interscapular region, though none had been there the day before. Two days after the injection there was an increase of sputum. Several days after the last injection the sputum was blood-streaked; this was during menstruation, and she had frequently seen blood in the sputum before the onset of her menses. On February 23, a third dose of 16 mg. was given, which was followed by some headache and increase in the bacillary content of the sputum. March 9, 16 mg., followed shortly by headache and flushing of the face, which lasted all day, though there was no rise in temperature or pulse. The next day the leucocytes were found to be increased; some increase in the cough and traces of blood in the sputum. March 22, 12 mg., without any evidence of reaction. April 6, an *x*-ray plate taken showed practically no change in lung shadows as compared with the previous plate. She had recently developed some edema of the ankles. On April 15 the bacillary content was Gaffky 2, and there had been a slight increase in sputum. The edema was decreasing, though at times she suffered with palpitation and orthopnea, and on one occasion had a rather sharp attack of precordial pain. On the evening of April 29 she had a brisk hemorrhage, 80 c.c. On May 1 another, 60 c.c., and on May 3 still another, amounting to 100 c.c. Since that time there had been no further hemorrhage. It will be noted that these hemorrhages came on after an interval of about five weeks following the last injection.

During the treatment this woman's weight increased from 117 pounds to 134¼ pounds. This exceeded her highest weight before illness by 5 pounds. Her general condition was very much improved, although probably her improvement was no more marked than on her previous discharge. Very little general reaction followed the injections, but focal reactions were frequent, occurring principally as pain in the chest. After the second injection there was a definite increase in the extent of rales. She ran practically an afebrile course throughout. Bacilli were still present after the last injection.

Case IX.—Thomas D., an Irish lumber-jack, age 36, entered the San Francisco Hospital January 16, 1917, complaining of cough, weakness, loss of weight, slight hemoptysis, and an ischiorectal abscess, which ruptured spontaneously a few days later. He had been a heavy user of alcohol. Denied venery. He had had pleurisy two years before and had lost 10 pounds in the past year. Since his pleurisy he had had constant cough, with occasional pain in the chest. Bacilli were found in his sputum one month before entrance. There had been several small hemorrhages since his entrance.

Examination showed a very well developed man, not appearing very sick. The extremities were slightly cyanosed. There was extensive bilateral tuberculous involvement, dullness extending to the fourth rib on either side, with rales almost to the base in both lungs. Although the heart was somewhat enlarged, there were no murmurs. The pulmonic second sound was accentuated. There was a slight amount of sclerosis of the peripheral arteries. The *x*-ray plate showed extensive mottling throughout both lungs, less marked at the bases, with fibrosis at both apices. Blood pressure, 110, 60. The rectum showed a discharging ischiorectal abscess. The urine was negative, with a phenolphthalein function of 50 per cent. Blood and Wassermann were negative. Tubercle bacilli in the sputum, Gaffky 4.

Treatment: Treatment was commenced January 29, 1917, 14 mg. being administered intravenously. This was followed by a slight increase in the cough and sputum, but no increase in rales. On February 12, 19 mg. given. The following night there was some cardiac irregularity, but no other evidence of general reaction. The next day a careful search of the sputum failed to reveal any tubercle bacilli,

a gain in weight was recorded, and there were fewer rales. The ischiorectal abscess looked cleaner, and the patient was generally feeling very well. February 26, 18 mg. followed by considerable perivascular infiltration at the site of injection, causing some pain. No general reaction followed this injection. There was a slight increase in rales and sputum. Two days after the injection he left the hospital without permission.

This man's weight increased from 156¼ pounds to 162 pounds during the treatment. As he left suddenly, there was no opportunity for examination at the time.

Case X.—Luella D., age 49, married, native of the United States, entered the San Francisco Hospital December 23, 1916, complaining of cough, pain in the chest and occasional night sweats. A sister had died of tuberculosis, and a brother and three sisters had died in infancy. She had had scrofula at two years of age, typhoid at fourteen, pleurisy at thirty; at about that time she was operated upon for mastoid trouble, the wound of which has never entirely healed. From that time on she lost in weight, suffering at times from stomach trouble, accompanied by cough. Three months before, during sharp pleuritic pains, tuberculosis had been diagnosed. She had always been delicate and subject to frequent and protracted colds. She had been married at sixteen, and three children had died of whooping-cough in early childhood.

Examination showed a woman wasted and bedridden, with a suppurating scar over the right mastoid, chronic pharyngitis, bad oral hygiene. Both upper lobes were involved in a tuberculous process, with considerable cavity formation in the left upper lobe. The *x*-ray plate showed extensive mottling throughout the left upper lobe, with probable large cavity under the clavicle. There was less involvement of the right lung, but there was rather a dense apical shadow and marked peribronchial thickening in the right lower lobe. The heart was ptosed. Tubercle bacilli were present in the sputum. The urine, blood and Wassermann were negative. Blood pressure 110, 72. Prognosis was bad, in fact, death seemed imminent.

Treatment: On February 1, an injection of 12 mg. was given, without reaction. On February 15, 16 mg. injected, followed the next day by slight increase in leucocytes. On March 1, following an injection of 12 mg., there was a slight chill, and the day following the bacilli were slightly increased. On March 15, 12 mg., with focal reaction the following day, shown by increase in rales, bacillary content of sputum and cough. The next day she felt very well. March 29, 14 mg. administered. This was followed by some distress in the chest and some increase in cough. The bacilli disappeared after this injection and were absent from the sputum until May 1, when they were found again in numbers amounting to Gaffky 2.

She increased in weight from 86¼ pounds to 91¾ pounds during the treatment. Examination of the chest on April 27 showed very little change in the physical signs, except that the signs of cavity in the left upper lobe were not as distinctly marked as before. The rales were less abundant, fibrosis and drying up of the cavity secretion had apparently been progressing satisfactorily. The amount of sputum and bacilli, however, were practically unaltered. The general condition was much improved; her appetite was good, she was hopeful, and was convinced that she had derived much benefit from the treatment.

Prognosis for improvement much better than at the beginning of treatment.

General Reaction.—There was little evidence of general reaction in the patients above recorded. Five cases experienced chills, four following the first injection, one following the fourth. These chills were in no instances

severe and seemed to have no relationship to the amount of the preparation used.

Rise in Temperature: This was unusual. There do not appear those sudden rises similar to what is occasionally seen following tuberculin administration. Two cases, I and VI, had slight temperature increases. In case VI it followed a dose of 21 milligrams. It was accompanied by a slight rise in the pulse rate and the number of leucocytes. It subsided again in four days. In two cases, V and VII, the temperature rose steadily and was higher at the end than at the beginning of treatment. Most of the patients were, however, afebrile throughout.

Effect Upon the Pulse Rate: Cases I and VI had increase in pulse rate, accompanying rise in temperature above mentioned. Some arrhythmia was noticed in Case IX, following his second injection of 19 milligrams.

Other evidence of general reaction was rare. The leucocytic curve was as frequently decreased as increased. Headaches were observed but usually in cases where headache was a frequent manifestation in the interval between injections. Particularly was this noticeable in Case VIII. Headache, malaise, insomnia, loss of appetite followed the large amount (21 milligrams) given Case VI at his third injection. These symptoms persisted for several days following.

Focal Reaction.—Evidence of focal reaction was very frequent, and was present to a greater or lesser extent in all cases save the one who died. This was indicated in various ways.

Probably the most marked focal reaction was seen in Case VII, where the morning following the first injection of 12 milligrams the entire left side of the chest was filled with moist, sticky rales, replacing the previous crepitation. Hoarseness, almost to aphonia, was also present and the arytenoids were much swollen. These evidences of focal reaction persisted for more than a week. Similar, though not as severe, reactions followed the second injection given this patient. All the cases, except the fatal one, showed increase in rales after one or more injections, but none to the same extent as Case VII. It usually occurred when doses of more than 12 milligrams had been given.

In the majority of the cases there was increase in cough following the injection, sometimes so severe as to require heroin for its relief. This was in quite a number of instances accompanied by an increase in the amount of sputum, and frequently traces of blood appeared. No brisk hemorrhages occurred, except in Case VIII, and in this instance it appeared more than a month after the last treatment. She had, however, a history of several severe hemorrhages before admission.

Sputum was carefully and frequently examined during treatment with reference to bacillary content, the Gaffky scale being used for this pur-

pose. No definite results were derived from this, the count decreasing in as great a number of cases as it increased.

There was pleural pain following most of the injections, sometimes very severe. This usually occurred with the other signs of focal reaction, but frequently it was present as the only evidence.

None of the patients had demonstrable pleural effusion except Case II. Six days after his fourth injection of 12 milligrams, spontaneous pneumothorax occurred on the left side. It was ushered in by a sharp rise in temperature, increased pulse, a slight increase in sputum, and much pain and dyspnea. The next day the sputum had materially diminished. This was followed in a few days by a pleural effusion which gradually absorbed. His temperature remained high for more than two weeks, when it subsided to a point slightly above normal.

General Condition.—All of these patients except Case II showed some increase in weight; not marked in any except Case VIII, the hemorrhagic one, who increased from 117 to 134¼ lbs., which is five pounds above her highest weight before illness. Of course, no deductions can be drawn from Cases III and IX, who left the hospital after receiving three injections each. It is significant, however, that in the first instance there was a remarkable improvement in his general condition, and after the focal reaction following the second injection, the cough and sputum entirely disappeared.

Most of these patients, in fact, all of them, now under observation except the one who had the severe focal reaction following the first injection, and with whom the prognosis was decidedly bad at the start, lay claim to a feeling of improvement and well-being entirely irreconcilable with the physical findings. This is not surprising to any observer who has had much experience with the tuberculous. Aside from the benefit naturally resulting from bed treatment and careful nursing to which these patients were subjected, the importance of psychotherapy in tuberculosis has long been recognized. This fact has been seized upon and illegitimately exploited by quacks for many years. The most glaring instance of it occurred a few years ago, when the profession complacently allowed the Friedmann fiasco to be perpetrated upon large numbers of these sufferers. I had the privilege at that time, through the courtesy of Dr. Stimson of the United States Public Health Service, of examining a considerable number of these patients. The optimism of these sufferers in the face of rapidly progressive destructive lesions afforded as pathetic a picture as could be drawn before the medical mind of the vicious results of conscienceless press advertising.

As a result of these observations, which by reason of the comparatively short time they have been studied, must be looked upon as a preliminary report, the following conclusions would seem justifiable:

(1) Copper and potassium cyanide in amounts from 8 to 12 mg.

in cases of uncomplicated pulmonary tuberculosis is not followed by injurious results.

(2) Large doses, or even smaller ones in complicated cases or those presenting extensive active lesions with fever may produce serious focal reactions causing permanent harm.

(3) Severe hemorrhages are not likely to occur.

(4) Its administration is not followed by severe general reactions.

(5) The preparation is not very irritating to the perivascular tissues if small amounts are accidentally injected into them.

(6) The value of the preparation in the treatment of pulmonary tuberculosis has not been conclusively demonstrated.

(7) Its further trial in the treatment of this disease is justifiable.

THE THERAPEUTICS OF URANIUM NITRATE

BY REYNOLD WEBB WILCOX, M.D., D.C.L.,

NEW YORK.

President of the American College of Physicians.

Uranium, a mineral long known in pitch-blende, was isolated in 1789. It was so named from the Greek *σὐρανός*, the sky, in allusion to the planet. Uranus. Uranii nitras,—uranium nitrate,—of the ninth edition of the United States Pharmacopœia contains not less than 98 per cent. of uranyl nitrate $UO_2(NO_3)_2CH_2O = 502.62$.

Source.—From pitch-blende which is an impure uranoso-uranic oxide or from uranite. Either of these, finely powdered, is treated with nitric acid, and various associated metals as lead, barium, bismuth, iron, zinc, radium, and polonium having been removed, uranium nitrate is crystallized from an aqueous solution.

Characters.—Light yellow prisms; odorless and having a bitter, astringent taste; somewhat efflorescent; radio-active emitting alpha rays and producing a new radio-active element known as uranium-x, resembling thorium, and which emits beta and gamma rays.

Solubility.—In 1.2 parts of water at 25° C. (77° F.); freely soluble in alcohol or ether.

Impurities.—Alkaline earths, heavy metals, iron, manganese, zinc, uranous compounds, sulphates.

Dose, 0.01 gm. = 10 milligm. (1/6 gr.).

Action of Uranium Nitrate.—Uranium nitrate is less radio-active than metallic uranium and some of its salts, but probably this effect is overshadowed by the other manifestations produced by this substance. Its systemic action is similar to that of other metals with an especial paralytic effect on respiration. It is very corrosive and highly toxic.

Kidneys.—In considerable doses in some animals, when injected intravenously, it produces degeneration, necrosis and desquamation of the tubular and glomerular epithelium with characteristic hyaline droplets in the wall of the capillaries of the glomerular tufts, which are not found in other vessels of the kidney or in other organs. There is, however, no hematuria, in spite of the marked congestion. It generally sets up an albuminuria and glycosuria with possibly an acetonuria, with torpor, somnolence, paralysis, collapse and coma. The glycosuria often develops upon the second or third day of intravenous injection. This may be due to increased permeability of the kidney, for it may appear

without any hyperglycemia, indeed uranium salts may even relieve an hyperglycemia if this should be due to a diminished permeability of the kidney. On the other hand, it may of itself produce a hyperglycemia, even if the kidneys be excised, thus pointing to an action which is entirely outside of the kidneys.

The excretion of albumin runs fairly parallel to that of glucose. It has also been noted that nephritic glycosuria and hyperglycemia occur after the administration of many substances, which are toxic as regards the kidneys, such as cantharides, which increases permeability of renal vessels, and chromium, tellurium, mercury, and aloin which cause lesions of the tubular epithelium. The urine is usually alkaline and slightly increased in quantity and in specific gravity for a short period; then it is diminished and when coma supervenes, anuria from obstruction of the tubules by edema and desquamation of cells, is complete. The coma is usually without convulsions unless they are of uremic origin. Repeated injections of small doses result in chronic interstitial nephritis with fibrous changes similar to the chronic diffuse nephritis found in man, but not identical with it for it is not associated with arterial lesions.

The toxicity of uranium salts is probably associated with acidosis because the administration of sodium carbonate lessens this and, as well, diminishes the degeneration of the renal epithelium. The oxaluria present indicates the poisonous effect of uranium and, with the emaciation, denotes impaired nutrition.

Blood.—The blood is rendered less coagulable, although it is not known by what means this is brought about. It also interferes with the restoration of the volume in the blood after saline infusion.

Respiration.—This is at first increased in rate and later becomes slower, while the pulse becomes more rapid, the blood pressure is raised through stimulation of the vasomotor center, and as asphyxia supervenes the temperature is subnormal. Respiratory paralysis causes death.

Alimentary Tract.—There is likely to be thirst, nausea, and vomiting with constipation and later diarrhea. It inhibits the production of ptyalin, pepsin, and trypsin, and its deleterious effects on digestion appear after hypodermatic as well as after oral administration.

Nervous System.—The somnolence, weakness of muscles, and paralysis are usually not marked until a few days before the death of the animals subjected to experimentation.

Anasarca.—As early as 1854 Leconte noted a peculiar dropsy resulting from the administration of uranium salts and this was again studied by Richter in 1904. The anasarcous and ascitic fluid is highly albuminous and is a transudation into serous cavities and into the tissues and may even affect the *fetus in utero*, as was noted in 1905 by Bibergill.

This condition is not explicable on the theory of nephritis resulting in anuria, but is probably one due to an altered permeability of the walls of the capillaries, according to the observations of Richter in 1904. This occurs only when animals have been freely supplied with water, otherwise anuria without dropsy will supervene.

In all the animal experimentation it has been noted that dogs, especially the older ones, were more resistant to the action of uranium salts than were rabbits. So far as animal experimentation has gone the intravenous administration of uranium salts produces a characteristic nephritis, glycosuria, and a peculiar edema.

The action of uranium salts seems to have attracted the interest of laboratory workers for a considerable period of time. Among those who have contributed to the pharmacology may be mentioned: 1824, Gmelin; 1851, Leconte; 1888, Chittenden; 1889, Chittenden and Lambert; 1890, Woroschresky; 1904, Richter; 1905, Bibergill; 1906, Fleckseder; 1907, Fleckseder, Hemmeke, Myerstein; 1909, Dickson; 1910, Jackson; 1911, Smith, Pollak, Christian; 1912, Dickson, MacNider; 1913, Franke, MacNider, O'Hare; 1914, MacNider, Myer, Lozzati; 1916, MacNider, Bogart, Underhill, and Mendel.

Therapeutics of Uranium Nitrate.—It has been used in England as a spray for the throat in 2 per cent. solution, with caution, for various conditions.

In 1895 Samuel West published the results of his observation of two patients suffering from diabetes mellitus; one a lad of twenty-two years, the other a woman of forty-five years. Later in the same year he added the records of one hospital and some other patients, but without complete details. He employed at first uranium nitrate and the double chloride of quinine and uranium, but finding no difference between the two salts, finally decided upon the former as equally efficacious. He was apparently familiar with the observations of Chittenden upon the inhibition of the activity of ptyalin after small doses of the drug and in larger quantity its effect upon pepsin and trypsin. He found that the drug, when administered by the mouth, acted slowly and that small doses (one-sixth of a grain) were as efficacious as larger ones (one grain), and finally that some tolerance of the remedy was apparently established.

He concluded that the general effects were as follows: After a short time all patients reported that their thirst was greatly relieved and that the frequency of urination and the quantity of urine was greatly reduced. If the sugar is largely influenced by diet the remedy is most useful on account of its physiological effect in digestion. If dieting and ordinary treatment have produced all the results of which they are capable, further improvement takes place after the administration of uranium nitrate. This result may be due to the slowing of digestion of starches

and some forms of albumin, and the remedy may be especially useful in controlling excessive pancreatic digestion.

No uranium is found in the urine, probably because none gets into the general circulation. It may, however, pass from the intestines to the liver and, having been excreted in the bile, again pass into the intestines. Although the author recognizes the fact that when it gets into the blood after hypodermatic injection it is an active poison, he believes that when introduced into the stomach it is not toxic because of its imperfect solubility and absorption. He reports that he has administered from fifteen to twenty grains, thrice daily, without symptoms of gastric irritation.

His method of administration was as follows: Commence with a small dose—one or two grains—and increase slowly after an interval of a few days until the desired effects are produced. The remedy is best given freely diluted with water, after food. He never observed any disturbance of digestion nor irritation of the stomach or of the bowels, nor that its prolonged administration caused glycosuria. The statements made by other authors, that it reduces hemoglobin and therefore the oxygenating power of the blood, were apparently not confirmed by the author, since he makes no mention of such results.

In the treatment of diabetes mellitus I have long since abandoned a strict antidiabetic diet excepting for experimental purposes while determining the character and severity of the disease, which should be considered rather as a symptom-complex of which persistent glycosuria, polyuria, thirst, emaciation, and weakness are prominent manifestations. On a diet as near normally balanced as is possible, due regard being paid to total quantity of food-intake, the dangers of excess of proteids, as indicanuria, purinemia and autointoxication on the one hand, and from lack of sufficient carbohydrates, as acetonuria and coma, on the other, are avoided. If the nutrition of the patient can be maintained, infections such as tuberculosis and septic conditions, as well as gangrene, are exceedingly rare. So far as drugs are concerned, their use is largely symptomatic; the opiates, and particularly codeine, the organic bases and nitrogen-benzine derivatives, especially antipyrine, and the volatile oils acting chiefly on the central nervous system, as valerian, all have their uses but are not to be considered as constituting treatment. Benzosulphinide is, of course, a condiment and should be used in much smaller amounts than is ordinarily directed, not because it is harmful, for it is not, but for the reason that smaller amounts are quite as efficacious and satisfying as sweetening.

The arsenic-lithium carbonate ordinance in carbonated water, devised by my old teacher, Martineau, which I learned while a student in Paris in 1882, is probably more frequently useful than any single medication, and particularly in diabetes mellitus of hepatic origin.

Patients suffering from diabetes mellitus treated with discrimination

after a thorough study so that the cause shall be accurately determined do not die from the disease or its ordinarily associated sequelæ. My oldest patient has been under my care for thirty-two years and has now reached the age of fifty-four. Often months pass without glycosuria or possibly with only traces of glucose in the urine.

On looking over my practice for the past twenty years I find one hundred and eleven instances of the various forms of diabetes, classified as follows:

Diabète azoturique.—If one considers the pharmacology of uranium, by analogy it should be influenced by this remedy. As a matter of fact, of seven patients suffering from this disease, none were benefited, and presumably the drug was without effect.

Diabetes alterans.—Three patients received uranium nitrate as a part of their treatment, but without any appreciable results.

Diabetes mellitus.—Nine of the neurotic type were apparently uninfluenced, as to their glycosuria, by the remedy. Of the hepatic type, fifty-four received the remedy, including six (three pairs) of the conjugal variety, and forty-six apparently received benefit in that thirst, polyuria, and glycosuria were improved, but generally only so long as the remedy was continued. The usual daily amount administered was from one-half to one and one-half grains; on a few occasions it reached three grains. Pancreatic diabetes naturally varies within wide limits owing to the diverse conditions affecting the gland. Of twenty-seven patients, twenty-two were improved as to the symptoms above noted, temporarily at least, but it was with difficulty, if at all, that any really lasting benefits could be obtained.

Diabète bronzé.—In two instances, in which uranium nitrate was employed absolutely no results were obtained. Of the infections, those due to syphilis, as paresis or tabes, or disseminated sclerosis, the disease seemed to be of more importance than the glycosuria, and no use has been made of the remedy. No patient under my care suffering from exophthalmic goiter has ever shown diabetic symptoms or signs, therefore no observations upon the effect of uranium nitrate have been made. Nor have I ever encountered diabetes as a sequela of typhoid or relapsing fever, or of cholera or diphtheria.

Diabetes insipidus.—Nine patients who have been under observation received uranium nitrate in daily amounts of from one-half to one grain. There was no reason why this remedy should influence the polyuria, and as a matter of fact it did not. In a disease of so obscure an origin and of so unsatisfactory a course and so little amenable to treatment one sometimes yields to temptation and embarks on therapeutic adventures.

In all the instances in which I have employed uranium nitrate I have never noted any untoward gastric or intestinal symptoms nor any signs

of blood or renal disturbances; careful observation has been especially directed toward the early detection of the latter. In some instances, especially in the hepatic and pancreatic forms of the disease, the remedy, when its use has resulted in the diminution of glucose to a trace or to total absence, has been continued for months and, for some patients, for years.

In conclusion, I believe that the statement as to the therapeutics of uranium nitrate, which I quote from the tenth edition of my Materia Medica and Therapeutics, is a fair one: Internally it has been employed with good effect in the treatment of diabetes mellitus for at least two decades. It will at times markedly diminish the amount of glucose in the urine, and this diminution, often to traces, will persist so long as the remedy is continued. In other instances it is entirely without effect. Its use then is purely empirical, without any basis for an opinion whether it will or will not be useful. Indeed, when its use is successful in reducing glucose, lessening thirst, weakness, and emaciation, there is no valid explanation of its action.

Fortunately in diabetes the urine is frequently examined so that structural changes in the kidneys are readily and early detected and the treatment at once abandoned. The digestive disturbances also give early and emphatic warning. On the other hand, it has been administered in large doses, and over long periods of time, even years, without any digestive symptoms or renal signs, with apparently great benefit to the patients suffering from actual diabetes mellitus.

TREATMENT OF HAYFEVER AND ASTHMA BY PITUITRIN AND EPINEPHRIN

BY ERNEST ZUEBLIN, M.D.

CINCINNATI, OHIO.

Associate Professor of Medicine, University of Cincinnati; Medical Director, Cincinnati Tuberculosis Hospital.

In a former communication (Medical Record, March 3, 1917), I published favorable results obtained by treating asthma cases with pituitrin and adrenalin injections. Since then several cases of hayfever have come under my observation in which a similar treatment was applied with good results.

I need not enter upon a detailed discussion of the etiological factors which are closely related to the current conceptions of immunization and anaphylaxis. Clinical and therapeutic experiences have established the fact that certain individuals present a hypersensitiveness to the pollen of certain blooming plants. These irritating substances gaining access to the respiratory tract are considered the cause of the well-known and distressing clinical symptoms, whilst vaccination with pollen extract seems to attenuate or to prevent the occurrence of the clinical manifestations. The therapeutic results with pollen vaccination are doubtless a great achievement in the relief and removal of the abnormal clinical signs. From the clinical standpoint, cases of hayfever offer much interest, since closer examination reveals certain clinical particularities which deserve our attention, as shown in the following cases:

CASE I.—Mr. W. B., age 36, teacher, negative family history and past history. Hayfever attacks date back for the past 18 years, which manifestations are of extreme violence, attended by burning, tickling sensations in the nostrils, eyes, throat, violent sneezing, serous discharge from the mucosæ of the respiratory tract, with distressing attacks of asthma—particularly in the evening. The exciting causes of such manifestations are the following: Blooming lilac, different gramineæ, roses, dusty, heavy, damp atmosphere. Patient before coming to me had tried all kinds of treatments for nose and throat and various drugs without any success whatsoever.

The results of the physical examination are the following: Patient short built, well nourished, eyes injected, abundant mucous nasal discharge; emphysematous chest, moderate harsh breathing over right apex anteriorly; numerous sibilant râles over both upper lobes anteriorly and prosteriorly. Heart, apex in left midclavicular line, fifth interspace; absolute cardiac dullness extending from fifth interspace to upper border of third rib, and slightly outside of the left sternal margin; relative cardiac dullness extends from fifth interspace towards the right and overlaps the right sternal border, reaching as far as the upper border of the second rib. Heart sounds:

Over mitral area first sound normal; tricuspid and pulmonary sounds weak, not accentuated; second aortic sound weak. Blood-pressure—auscultatory method—Tycos —112 systolic, 78 diastolic; 34 pulse pressure. Abdomen prominent, nothing particular. Knee-jerks accentuated. Marked dermography of the skin.

Treatment and clinical remarks: Subcutaneous injection of pituitrin, 1 c.c.; Adrenalin chloride solution 1/1000, 0.5 c.c., given on June 6, 1914. Patient reported two days later, felt very well after the injection; came down town in motor car; experienced slight tickling in the nose, dryness, and some watery feeling, but had no sneezing or any further unpleasant manifestations. Since this was my first hayfever case, as a precaution the patient was given one dram t.i.d. of the following prescription: Ammon. iodide, ʒj ss; ammon. bromide ʒii; tincture lobelia, ʒj; syrup of tolu, fl. ʒij; peppermint water, q. s. ad. fl. ʒiij. Alcohol rub for the skin every morning. June 11. Notwithstanding the hot and close weather and blooming grass, which factors always caused a severe hayfever attack, the patient experienced only a slight tickling sensation in the nose, which lasted for about 5 minutes instead of several hours as in former times. No attacks of sneezing whatsoever. Pulse 81. Blood pressure: Systolic 108, diastolic 70; pulse pressure 38. Patient received another injection of pituitrin and adrenalin in the dose mentioned above. Reported at office 3 days later that he had been feeling fine for two days after the injection. Slight sneezing and burning sensation was noticed during an exceedingly damp, moist and rainy day, but no discharge from nose, and no dyspnea. The injection was repeated without any internal medication, which was discontinued. The fourth and fifth injections were given on June 17 and 22. The weather conditions were the same unfavorable ones as mentioned all the time, but no single attack, no dryness, no sneezing and no discharge whatsoever was recorded by the patient when last seen on July 6, at which time the sixth pituitrin and adrenalin chloride injection was given. The patient was advised to report at the slightest indication of a hayfever attack but no such occurred, whilst all the previous years the severe attacks lasted for three months, with daily paroxysms.

The patient kept well throughout the summer of 1914 and only reported the next year on June 5, 1915, on account of a moderate dry sensation in his nose, with tickling, signs which were always infallible for a hayfever attack. No sneezing spells nor dyspnea were noticed so far. As the only objective signs of interest the heart examination must be recorded, namely, dilatation of the right ventricle—threshold percussion—muffled first mitral sound, relatively small pulse pressure. The extent of the absolute cardiac dullness: apex sixth, interspace, slightly outside of midclavicular line, reaching to lower border of third rib and the middle of the sternum. Relative cardiac dullness extends from the sixth interspace towards the right, overlapping for one inch the right sternal border, reaching upward to the upper border of the third rib. The diameters are for the transverse diameter 5¼ inches, oblique diameter, 5¾ inches; height, 4¼ inches; the surface area of the relative cardiac triangle measuring 11.65 square inches. Heart sounds indistinct, muffled first mitral sound, second sound very distant, accentuation of both second aortic and pulmonic sounds; first tricuspid sound split, roughened, but no murmur. Pulse weak, irregular, becomes faint during bulbous pressure, the rate 78; after pressure is relieved slows down to 66; blood-pressure systolic 106 mm., diastolic 78, pulse pressure 30 mm. Hg. pressure pro one minute 14,560 mm. Few scattered dry râles over the pulmonary hilus posteriorly and in front. Marked dermography, considerable flushing of the skin, conspicuous indicanuria being present.

Treatment and clinical remarks: On June 5, 7, and 9, subcutaneous injections of 1 c.c. pituitrin, and 0.5 c.c. of adrenalin chloride 1/1000 were given, and for 4 days 2

minims of the following solution: Atropine sulphate, gr. 1/40; peppermint water, ʒij. The therapeutic results are summarized as follows: The heart sounds became absolutely normal following the second injection, the heart showing on threshold percussion a lessened transverse diameter, 3⅜ inches—1⅞ inches less; height, 2¼ inches—2 inches less; oblique diameter, 4 inches—1¾ inches less than on the previous examination. The pulse and blood pressure figures and lmin. Hg. pressure were found on June 7: 90 pulse, 120, systol. 92. diastol. pulse pressure 38. 19,080 mm. Hg. pressure pro. 1 minute. June 9: pulse 90, 120 systol. 80, diastol, 40, pulse press. 18,000 mm. Hg. pressure pro 1 minute. June 11: pulse 80, 118, systol. 70, diastol. 48, pulse press. 15,040 mm. Hg. pressure pro 1 minute.

Very damp and close weather prevailed. Except a very slight tendency towards sneezing, no typical hayfever attack occurred throughout the entire season and also during the next year, 1916, the patient was reported perfectly well without having experienced any of his former paroxysms.

Case II.—Miss M. K., age 53, school teacher and secretary, reveals a negative family history, mentions in her past history otitis media with remaining deafness following measles; subject to rheumatism during the past 5 years, with stiffening of the fingers and knees. The attacks of hayfever started 20 years ago, returning with great intensity in May every year, lasting for about 8 weeks. The first paroxysms were noticed 20 years ago, whilst spending a pleasant day out in the country in the season of roses. Patient mentions the following symptoms: Sneezing, redness, serous discharge from the eyes, raw feeling of the mucous membrane, cough, cold in the head, rendering nasal breathing impossible, severe attacks of asthma at rest and after exertion, occasionally occurring during the night so that the patient had to get up for relief. These attacks were daily without any change in severity and duration. All previous treatment in former years consisting in nose and throat treatment, in local application of menthol; preparations of pollantin had no result whatsoever. Substances which are thought by the patient as causative factors are roses, timothy grass, dust from the street, from old papers, books, etc., seashore climate. Change of air to the mountains has no influence at all upon the course or intensity of these attacks, which are dreaded very much by the patient at the approach of the pollen season. Digestive functions are slightly impaired, heaviness, belching of gas after meals, acidity, marked constipation. Circulatory disturbances present, dyspnea after moderate exertion, emotional palpitations, perspiration. Tendency towards headaches, dizziness. Sleep good. Frequent eruption of hives, not dependent upon the intake of any food. When getting up patient frequently complains of a thick throat. Patient flushes easily, is subject to chilly sensations without any rise of temperature.

Physical examination of the short-built patient: Conjunctivæ moderately injected, tonsils irregular, not enlarged. Chest—lack of respiratory expansion of left, depressed apex, emphysema over remainder of chest, harsh granular inspiration over left apex anteriorly, the same character of breathing existing over both apices posteriorly with numerous, scattered fine crepitant râles, vocal fremitus normal. Heart—apex impulse fifth interspace, indistinct relative dullness in fifth interspace, 4 inches to the left, 1⅛ inches to the right from the midsternal line; height 3¼ inches, oblique diameter 5½ inches, cardiac superficial dullness, triangular content 8,328 square inches. Heart sounds—mitral first sound very indistinct, weak, resembling embryocardia, second sound also weak, not to the same extent. Over the other auscultatory areas the sounds are very distant and indistinct, no murmur nor accentuation of the second pulmonic sound can be found. Pulse 96, not well sustained, weak but regular as to rhythm. Systolic blood pressure 108, diastolic 82, pulse pressure 26, which figures were only obtainable by the palpatory, not the auscultatory method; total Hg.

pressure pro one minute 18,240 mm.; Hb. 65 per cent. Talquist. Urine:—spec. gravity 1,012, no albumin, marked indicanuria. Stomach:—testmeal withdrawn 4 hrs. after Leube-Riegel meal 48 per cent. free HCl, total acid 60 per cent. Abdomen and extremities normal. Treatment and clinical remarks—Pituitrin 1 c.c. and adrenalin 0.5 c.c. injections were started at once. The results are recorded below.

1915	Tr. D.	H.	Obl. D.	Surf. J Sq. in.	P.	S.P.	D.P.	Pp.	Hg-mm. Pro. 1′	Dose Inject. Pit. c.c.	Dose Inject. Adr. c.c.
	"	"	"								
May 13	5⅛	3¼	5½	8.328	96	108	82	26	18,240	1	1
May 15	3¾	2½	4½	4.687	81	114	64	50	14,418	1	0.8
May 17	...	...	...	....	81	112	68	44	14,580	1	0.5
May 19	4½	2½	4½	5.625	81	104	62	42	13,446	1	0.3
May 25	4¼	2½	5	5.3125	78	118	90	28	16,224	....	....
May 28	4¼	3	4½	6.375	78	116	88	28	15,912	0.8	0.4
May 31	3¾	2	4	3.75	97	112	76	36	18,236	0.8	0.4
June 2	3¼	2	3½	3.25	69	114	72	42	12,834	0.25	0.5
June 4	4	3	4½	6.0	84	112	76	36	15,792	0.8	0.4
June 7	4¼	2½	4½	5.31	88	122	78	44	17,600	1.0	0.5

On May 15, patient reporting at my office, slight discomfort was noticed at point of injection, moderate headache was present, but no other complaint. As seen from the table, the size of the cardiac dullness had changed considerably, slower pulse rate, better pulse pressure, heart-sounds, particularly the first mitral sound, were better sustained and accentuated. On May 17, no manifestations are reported, patient feeling stronger and well stimulated, the pulmonary findings reveal less moisture. Pulse is full and strong, no more burning sensations are noticed in the nose. Heart sounds are slightly diminished in intensity, patient is advised to take 2 minims t.i.d. after meals of atropine gr. 1/40 in peppermint water ℥ij. May 25, pulse is fuller and stronger, well sustained, patient is feeling excellent notwithstanding the murky weather, a high humidity, and abundant precipitation. Patient reports to have undertaken an automobile ride in the country, with much dust, which exercise in former years always resulted in violent hayfever manifestations, but such a result was not observed this time. Notwithstanding strenuous work at the office, sustained exertions connected with preparations for closing up the house before going West, the patient feels exceedingly well, as quite distinct from former years. The heart sounds are good, embryocardia has disappeared. The same report is given on May 28 and 31, and as seen from the table an attempt was made to decrease the dose of pituitrin, whilst digalen m. x, t.i.d. was tried in order that the patient who intended to go West should have a cardiac stimulant whilst exposed to exertion and excitement during her long travel. On June 4, a moderate increase in the size of the heart was found, with a lower pulse pressure, on account of which the dose of pituitrin was raised to 0.8 c.c. The digalen dose was reduced to m. viij, t.i.d. and also the atropine to m.j. The patient was seen on June 7 doing very well and presented at the examination of the heart well sustained heart sounds accentuation for the second pulmonic, higher systolic, a moderate diastolic, high pulse pressure, and a better Hg.mm. pressure pro minute.

The patient on her sight-seeing trip to San Francisco, notwithstanding unaccustomed exertions experienced only slight discomfort while touring in the Rocky Mountains. Some palpitation and cardiac oppression were noticed in climbing, which symptoms cleared away rapidly after rest.

The patient returned home in very good condition and was not heard of until June 5, 1916, when she was preparing to leave the city for her vacation. At that time, a few days preceding her call, irritation of the eyelids and nostrils, moderate watery mucous discharge from the mucous membranes, very moderate sneezing, but no respiratory difficulties were noticed. Again on physical examination the heart showed dilatation, muscular weakness, indistinct heart sounds, particularly both mitral sounds were found indistinct, murmurish, accentuated; split second aortic sound; low systolic, high diastolic and low pulse pressure. The figures of the diameters of the heart are given below, as well as those for pulse and blood pressure readings.

	Tr. D.	H.	O. D.	Surf. Sq. In.	P.	S.P.	D. P.	Pp.	Hg.l'P.	Inject. Dose Pit. c.c.	Ad. c.c.
June 5	5⅝″	4″	6½″	11.25	78	112	88	24	15,600	0.8	0.
June 7	4¼	3¾	5¾	8.43	75	110	74	36	13,800	1.0	0.2

The patient reported two days later following the first injection, feeling perfectly well, and objectively presented normal heart sounds, regression of the cardiac dilatation, lowered diastolic, increased pulse pressure, a smaller figure for the one minute mercury pressure. The results of the last injection could not be controlled by physical examination but the patient leaving the city for the South, notwithstanding very hot and damp weather, roses and other flowers in full bloom, was entirely free from symptoms suggesting her former "rose-colds." Whilst sojourning in New England during a wet summer, the patient reported that she had experienced only very slight discomfort of occasional watery discharge from her eyes and nose, but never any asthmatic attacks, which were so troublesome in former years. Since the patient was at my office only twice before starting out for her vacation, I had some doubt whether the two injections of pituitrin and adrenalin were sufficient to protect her from any further manifestations of her rose colds. If it could have been arranged to give the patient the pituitrin injections, it is my impression that even the slight manifestations mentioned above could have been averted.

Among my hay fever patients there are four more cases, two women and two men, who were treated by the pituitrin and adrenalin injections. Time, however, and space forbid me to enter into a detailed analysis of their cases. Briefly speaking, on first examination they all revealed dilatation of the heart, with weak sounds, rapid pulse, low systolic and high diastolic blood pressure, low pulse pressure, digestive disorders, particularly marked indicanuria. Under pituitrin and adrenalin injections these cases showed all at least reduction in the size of their heart, better heart sounds, improved blood-pressure findings; symptomatically the attacks did not return, or were lessened in intensity and severity. In giving my personal clinical observations on a few hay fever cases, I am fully aware that definite conclusions from the present observations should not be drawn. From the theoretical and clinical standpoint two points seem of interest, namely:

1. That the symptoms emanating from the respiratory tract are probably not the only ones present; that, at least as shown in the cases referred to above, there may be found definite signs of a cardiovascular

deficiency-cardiac dilatation, weak heart sounds, abnormal blood pressure findings, vasomotor weakness, associated with indicanuria of nutritional or intestinal origin, which functional disturbances may be favoring factors for the manifestations resulting from the pollen irritation. Somewhere, somehow, the pollen floating in the air must reach the mucous membrane. Admitted the lack of a vasomotor tonus, a low circulation, and weakened heart condition, the possibilities are that the irritation of the pollen is more apt to cause the distressing clinical symptoms.

2. That from the therapeutic standpoint pituitrin administered in appropriate doses may remove the cardiovascular depression and in some instances cure, or at least alleviate, the clinical symptoms. The making of such a statement does not imply that pituitrin medication is the only substance to be used in hay fever cases, nor does it mean that the pollen vaccination is out of place. As said before, the vaccination treatment has its usefulness and is apt to secure good results. From the clinical standpoint I believe that the attendant signs of vasomotor and cardiac weakness ought to be considered in the outline of treatment for hay fever cases.

Admitting that the posterior part of the pituitary body plays a more important part in human physiology than generally supposed, especially with reference to the vagus nerve, it is at least probable that by the proper therapeutic use of pituitrin we are able to help the patient and secure him better protection from the tedious symptoms attributed to hay fever.

PRESENT STATUS OF VACCINES AND SERUMS WITH REFERENCE TO PROPHYLAXIS AND TREATMENT

BY FRANCIS EDWARD STEWART, PH.G., M.D., PHAR. D.

When Kircher, in 1659, and Leeuenhoek in 1675, experimenting with lenses discovered the unseen world of microorganisms, they opened the door of two new sciences—the science of bacteriology and the science of immunology. Both of the sciences have developed into rapidly growing and important branches which have revolutionized our knowledge in almost every department of life, and made great changes in our ways of living and in civilization itself.

The subject of my paper has to do more particularly with the influence of bacteriology and immunology upon medical science and upon the arts of preventing disease and treating the sick.

The minute living organisms discovered by the early pioneers above mentioned, were at first called anamalculæ, but as knowledge concerning them developed they were later christened "microbes" from the Greek words, *micros*, small, and *bios*, life.

During the century following the work of these pioneers, the efforts of investigators were mostly directed to the morphology and classificatin of these minute living creatures. In the meantime, thinking physicians began to suspect the casual relationship of microbes and certain infectious diseases. Their constant presence in the tartar from the teeth, in the intestinal contents, in water, milk and food and in the dust floating in the air, was significant, but it was not until about 1850 that Pollender found minute rod-shaped bodies in the blood and spleen of animals dead of anthrax, which Davaine identified as the special virus of the disease. Anthrax or splenic fever was the first infectious disease scientifically demonstrated to be of microbic origin. Speaking before the French Academy of Medicine at this time, Davaine suggested that the phenomena manifested by animals sick of anthrax might be due to a specific fermentation produced by these microbes. The philosopher, Robert Boyle, working in the 17th century, had prophesied that the mystery of infectious disease would be solved by him who should explain the nature of fermentation. The discovery of the yeast plant by Cagniard-Latour in 1835 and by the botanist Schwann in 1837, and the demonstration that this plant causes the fermentation in beer and wine was confirmed by Helmholtz in 1843, but it was left for Pasteur to work out the problems of fermentation and connect up the germ theory of disease with the fermentation theory. His observations

were published in 1858, 1860 and 1863. More than half a century before the time of Pasteur, Jenner had succeeded in perfecting his method for vaccinating against smallpox. Pasteur, animated by the brilliant results secured by Jenner, discovered the reason why vaccination protects against smallpox, and also was able to demonstrate that other infectious diseases are preventable by the use of modified disease viruses, or vaccines as they are called.

The limits of this paper will not permit a detailed history of the rapid development of bacteriology and immunology resulting from the work of Pasteur and his followers. The germ of one infectious disease after another was discovered by these investigators, which in the brief space of 15 years explained the causation of the majority of infectious diseases and placed in the hands of the medical profession methods for the prevention and cure of many of them.

OPPOSITION TO VACCINES AND SERUMS

Immediately after Jenner's discovery bitter opposition arose to vaccination against smallpox. It was first claimed that the physical characteristics of the bovine species were transmitted with the vaccine and that the persons who submitted to it developed horns and hoofs like a cow. Thousands of circulars were sent out in England with an illustration of these remarkable effects. It was entitled "The Cow-Pox; or the Wonderful Effects of the New Inoculation." Equally foolish arguments are still being advanced by the anti-vaccinationists against the use of vaccines and serums. While it is admitted that no danger is to be apprehended of horns and hoofs growing upon those who are vaccinated, the anti-vaccinationists still maintain that the introduction of modified disease viruses, or vaccines, into the human body is fraught with danger to health and even to life.

One of the claims against smallpox vaccination is that tetanus frequently follows the operation. This objection was discounted by an exhaustive study on the part of the Bureau of Hygiene. The bulletin on this subject states that "It is difficult, even impossible, to produce tetanus in susceptible animals by vaccination with virus containing large numbers of tetanus organisms which have been purposely placed therein; that post vaccinal tetanus is very rare, only 41 cases being recorded in every 31 million subjects in 1904 to 1913 inclusive. The Bureau of Hygiene failed to demonstrate tetanus organisms in a large amount of vaccine virus specifically examined for that purpose, and decided that cases of tetanus occurring 15 or 20 days subsequent to vaccination did not receive their infection from the vaccine virus; also in all probability the infection is received about the 10th day; that tetanus not following vaccination is of far more frequent occurrence than post vaccinal tetanus. In 4 years the City of Philadelphia dis-

tributed 190,427 "vaccinations." Dr. Wadsworth, the coroner's physician, estimated that private firms sold at least double this amount, making more than two million vaccinations in this city. Tetanus followed in only 13 cases, while there were 90 cases of tetanus having no relation to vaccination.

DIPHTHERIA ANTITOXIN

Diphtheria antitoxin, or antidiphtheritic serum, has reduced the mortality of diphtheria from 40% to less than 20%. Dr. Jules Comby, in a paper read before the Fourteenth International Medical Congress in 1903, claimed that if diphtheria antitoxin is employed during the first 48 hours of the disease the mortality is abolished entirely. This conclusion seems to have been amply verified by other competent observers. It is well to record that post diphtheritic paralysis and other complications have been largely decreased by increasing the dosage. State Commissioner Dixon, of Pennsylvania, reports dosages of 52,000; 57,000; 63,000; 68,000; and 117,000 units resulting in recovery without renal or cardiac complications, and so far as he was able to ascertain, without recording any cases of post-diphtheritic paralysis.

TETANUS ANTITOXIN

Tetanus antitoxin has had a wonderful record during the present great world war. Early in the war the mortality from tetanus was a menace to the armies on both sides engaged in the great conflict. It has been stated that about 10% or 12% of all the wounded were attacked by the tetanus bacillus and about 90% of them died. The disease was controlled by tetanus antitoxin. Sir David Bruce of the British Army demonstrated that the protection afforded by single injections of tetanus antitoxin is not complete and therefore repetition of the injection at intervals of 7 days was recommended as a precautionary measure in order to keep up the protection. An initial dose of 500 units is usually given, the same dose being employed for the repetitions. Studies also were made by Col. Sir Wm. B. Leischman, Maj. A. B. Smallman and Capt. H. Burrows, of the Royal Army Medical Corps. It was incontestibly proved that a prophylactic dose of tetanus antitoxin not only has a really wonderful effect in preventing the disease and even in cases where the dose of antitoxin had been insufficient as a preventive but sufficient to modify the disease, almost as striking results have been obtained. Leischman and Smallman show that the death rate was very definitely less when the dose was given within 24 hours of the infection of the wound, as compared with the death rate in those cases in which the injection was given later. It was also shown that the danger of anaphylactic shock from the injection of tetanus antitoxin is negligible when the prophylactic dose is contained in such small quantity as 3 mil.

of horse serum, whatever the interval after the preceding injections. "Highly concentrated serum, in doses sufficient to maintain protection, may be repeated at weekly intervals as long as it is considered advisable, without any fear of the occurrence of anaphylaxis." In the treatment of tetanus when it has once declared itself, the intramuscular and subcutaneous routes should be selected in preference to any other, is the opinion of the editor of the Lancet, founded upon the work of Col. Leischman and Maj. Smallman. The dose should be not less than 10,000 units per day for the first few days. The mortality after doses of 20,000 units is less than when smaller doses have been given. The large doses of horse protein necessary for administration therapeutically may become the source of anaphylactic phenomena. This, according to Capt. S. Wyard, R.A.M.C., may be entirely avoided in the following manner:

"A small rectal injection of the serum should be given within 12 hours, which renders the individual safe from anaphylaxis no matter how large a dose is given subcutaneously; or, if this amount of delay is thought inadvisable, the same result can be obtained by a succession of subcutaneous doses beginning with a very small dose and rapidly rising to a large and efficient one."

The editor of the Lancet says that the observation of these precautions should be sufficient to remove all risks of anaphylaxis, and the fear of its occurrence can no longer justify the failure to employ protective serum in every case where it can possibly be of service. This of course applies also to the therapeutic use of the serum.

ANTIPNEUMOCOCCIC SERUM

Medical scientists (Avery, Chickering, Cole and Dochez) have proved that the pneumococci causing pneumonia can be divided into four classes, types or groups, according to their specific serum reactions, and under the head "pneumonia" at least four different pneumococcic pneumonias exist according to the type of pneumococci causing the disease.

The Rockefeller Institute shows that the percentage incidence of the different types of pneumococci in 100 cases of lobar pneumonia and the average mortality of those untreated with serum are approximately as follows: the figures indicate types of pneumococcus, incidence and mortality, respectively, the latter two figures being percentages: I-33-35; II-31-32; III-12-25; IV-24-16.

Type I serum is highly effective in the treatment of cases of pneumonia due to type I pneumococcus. The serum treatment of type II is much less efficacious. Type III antipneumococcic serum is slightly protective. The immunizing power of serum prepared by immunizing horses against type IV (group IV) pneumococcus has not been determined.

It has been proposed that immediately after admission to a hospital

or after coming under the care of a physician and before the type of infection is determined, every patient should receive a large dose of antipneumococcic serum of type I, or a polyvalent serum containing antibodies to types I, II and III pneumococcus. The object of employing this method is to avoid the delay incident to the determining of the nature of the infection. Patients treated under conditions where type diagnosis may be readily obtained should receive a large dose of type I serum promptly after the character of the infective microorganism is determined. Otherwise, the serum should be promptly given without diagnosis. As the polyvalent serum is standardized against type I pneumococcus, and is therefore of precisely the same potency as type I serum and contains antibodies to types II and III, many physicians prefer to use the polyvalent serum.

Every patient with pneumonia, immediately on admission to the hospital or coming under the physicians' care, should receive proper tests to determine whether hypersensitiveness to horse serum exists. With this object the patient should be first questioned for a history of previous injections of immune serum for diphtheria, meningitis or tetanus infections, also concerning previous symptoms suggesting asthma or hay fever since persons having such symptoms are likely to be sensitive to various proteins including those in the serum. The patient should be subjected to the intradermal skin test by injecting 0.02 mil. of sterile diluted horse serum (normal or immune) diluted with salt solution 1 :10, intradermally, that is, between the layers of the skin. A small white wheal about 3 m.m. in diameter, showing the little depressions of the hair follicles, is produced. An injection of a like amount of sterile salt solution is made as a control. It is advisable to make the serum and the control injections at one level on the forearm about 3 to 4 c.m. apart in order that the test may not be obscured by the possible spreading of the injected material along the lymphatics. If the test is positive, the wheal produced by the injection usually begins to develop within 5 minutes into a genuine urticarial wheal, which may increase slowly in size up to that of a half dollar, the wheal in turn being surrounded by a larger erythema. This lesion usually reaches its maximum within an hour and fades away rapidly, disappearing entirely in a few hours. In very susceptible persons this test may produce general symptoms, flushing of the face, increased rapidity of the heart movement and respiratory discomfort.

For purposes of desensitization, the Rockefeller Institute scientists consider it advisable to inject 0.5 to 1 mil. of antipneumococcic serum or sterile normal horse serum subcutaneously into every pneumonia patient as soon as the skin test is completed, even though the intradermal skin test is negative; "for occasionally one sees a patient in whom the skin test appears to be negative and yet in whom the injec-

tion of large amounts of serum slight symptoms of serum sensitiveness appear. It is believed that the subcutaneous injection of a small dose of serum will desensitize a patient for from 6 to 8 hours to several days. However, this procedure should not be relied upon to the extent of giving subsequent intravenous doses at a rapid rate."

In case the skin test proves positive, a more thorough method of desensitization is recommended. "This should consist of giving extremely small amounts of serum subcutaneously at ½ hour intervals, doubling the size of the dose at each injection." The subsequent use of the serum should begin with 0.25 mil. of serum to be followed in another hour by 1 mil., subsequent doses being given at half hour intervals beginning with 1.01 mil. and doubling the dose at each injection. After 25 mil. of serum have been given in these small doses, 50 mil. may be given at one dose after a lapse of 4 hours, followed by the regular dose 6 to 8 hours later.

As to the amount of serum to be given, it is recommended that the initial dose shall be 90 to 100 mil. except in cases where there is hypersusceptibility to the serum, as above stated, the dose to be repeated every 8 hours until definite favorable result has been obtained or there are indications to the contrary. The average total amount of serum required is generally 250 mil.

ANTISTREPTOCOCCIC SERUM

Much interest was excited in the subject of serum treatment in streptococcic infections by a paper contributed to the Society of American Bacteriologists, at the Eighteenth Annual Meeting, held in December, 1916, at New Haven, under the auspices of Yale University. The paper was entitled "Studies upon the Streptococcus" and was contributed by Dr. A. Parker Hitchens and his associates. Careful and elaborate tabulation of complement-fixation tests of 125 strains of streptococcus used for immunizing horses in the preparation of polyvalent antistreptococcic serum revealed the fact that there are about 15 strains with antibody-producing power far greater than that of the others. Antibodies produced by these 15 varieties were found to be polyvalent and capable of destroying all of the other types of streptococci. A serum prepared by immunizing horses with these 15 strains resulted in the production of a polyvalent antistreptococcic serum having a higher potency than that previously produced by immunizing horses with the entire 125 strains. This serum manifested a much higher immunizing power when injected into the human body than the serum prepared from all the strains.

What applies to antipneumococcic serum in regard to dosage and method of application applies with equal force to antistreptococcic serum. Brilliant results may be expected in a certain proportion of streptococcic infections when the serum is used in large doses early in

the case and continued in sufficient quantities and at proper intervals to maintain the antibody concentration of the patient's blood.

ANTITYPHOID VACCINE

The control of typhoid fever in the armies of the world by antityphoid vaccination and proper sanitation is so thoroughly established that I will omit further reference thereto. However, in this connection it is well to call attention to the fact that the campaign instituted against antityphoid vaccination two or three years ago, on the ground that the injections diminish the individual's resistance to tuberculosis, failed in its object. Major Russell, of the Medical Corps, U. S. Army, who had charge of the vaccination of the troops at that time, presented sufficient evidence to offset the claims of these anti-vaccinationists, which were sufficiently conclusive to set the minds of most students of the subject at rest. Further evidence has been presented by Baldwin and L'Esperance* who conducted experiments on guinea pigs with tubercle bacilli, and after they had become infected were inoculated with typhoid bacilli. It was found that the average duration of life of those vaccinated was 32 days longer than that of the unvaccinated animals. Even when the tubercle bacilli were given in overwhelming doses the vaccines had almost no influence on the length of life, the vaccinated animals living on an average of 7 days longer than the ones not given the vaccine. These experiments suggested that the beneficial effects obtained may be in part due to the stimulation of nutrition by the injected protein and in some way not primarily antibacterial. The recent experiments of Jobling* by injection of foreign proteins would favor this theory. Von Dungern's experiments are also confirmatory. He demonstrated beneficial effects on cases of anthrax following the injection of large doses of killed Friedlander bacilli. More recently Kraus** has shown marked improvement in cases of typhoid following the injection of large doses of colon bacilli, and typhoid vaccine gave marked benefits in certain pelvic infections.

A mixed vaccine prepared from the typhoid bacilli and paratyphoid bacilli "A" and "B" is being used in immunizing against typhoid fever. Dr. Aldo Castellani, Regius Professor of Tropical Medicine, University of Naples, not only advised the use of a mixed vaccine of this character for the immunization of troops, but also suggested and successfully used a vaccine containing in addition thereto, microbes causing cholera and plague, or Malta fever.

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*The Influence of Typhoid Vaccine on Tuberculous Guinea Pigs. Helen Baldwin and Elise S. L'Esperance. *Jour. Immunology,* Balt. 1917, 2, 283-299.

*Jobling & Petersen—"The Nonspecific Factors in the Treatment of Disease"—*Jour. A.M.A.,* June 3, 1916, p. 1753.

**Kraus, R., *Wien. klin. Wchnschr.,* 1915, p. 29.

ANTIDYSENTERIC SERUM

Dr. G. W. McCoy, Director of the Hygienic Laboratory, Washington, D. C., in his paper entitled "Usefulness of Serums and Vaccines Under War Conditions," published in the Journal of the A. M. A., May 12, 1917, says: "It is well known that dysentery organisms of the Shiga-Kruse type produce toxins and that it is possible to produce a serum which neutralizes these poisons. Evidence at hand indicates that such a serum should be tried in case of bacillary dysentery due to organisms of the Shiga-Kruse type. As high as 80 mil. have been given at one dose."

A polyvalent serum prepared from the several types of dysentery bacilli above referred to has been used quite extensively in the armies of Europe for combating bacillary dysentery, apparently with considerable success.

STOCK VS. AUTOGENOUS VACCINES AND SERUMS

The controversy between the advocates of stock and of autogenous vaccines still continues. The fact that antityphoid vaccine is a stock product, proves that vaccination against typhoid fever with a stock vaccine is of high immunizing value. Whether it is of equal value to an autogenous vaccine in the treatment of the disease is yet to be proved. The use of stock vaccines in staphylococcic infections is generally conceded to be satisfactory. In streptococcic infections, owing to the large number of strains of streptococci, an autogenous vaccine is probably to be preferred, although excellent results have been reported from the use of polyvalent streptococcic vaccine. Each class of infection is to be considered separately in this connection, although a general rule has been given by Allen* who says: "Generalizing, it may be fairly said that in chronic infections little will be lost by trying the effect of a stock vaccine before proceeding to the manufacture of an autogenous one, and that in severe acute infections much may be gained by administering a 'stock' vaccine while the autogenous one is in preparation. It is almost superfluous to add that if a stock vaccine is to be employed great care must be taken in the correct diagnosis of the infective agent, and that to this end due consideration must be paid to clinical and bacteriological evidence alike."

In relation to serums, they are of course stock products as a rule. The successful use of antibacterial serums is dependent upon the presence of antibodies of specific antagonistic influence upon the infecting microorganisms.

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*"Vaccine Therapy and Opsonic Treatment" by R. W. Allen, M.D., B.S., (London) 4th edition, p. 119—P. Blakiston's Son & Co.

SENSITIZED VS. NON-SENSITIZED BACTERIAL VACCINES

Besredka and Metchnikoff* suggested a plan of injecting a vaccine composed of living bacteria previously immersed in their specific immune serum, or, in other words, the use of sensitized bacterial vaccines. These authors first used both living and killed bacteria in the preparation of these so-called sensitized vaccines in the prevention and treatment of various infections. They claimed that both kinds of sensitized bacteria give good results as vaccines, but consider the living sensitized organism preferable to the killed sensitized organism.

A vaccine has been defined as a modified disease virus, so modified as to prevent destroying its power of infection, but not so modified as to destroy its power of stimulating the body cells of the vaccinated individual to produce the specific proteolytic digestive ferment to which immunity is due. Therefore the potency of a vaccine is largely dependent upon the precise amount of modification occurring during its preparation.

The reason why the vaccine prepared by sensitizing living bacilli is of greater potency than that prepared by sensitizing the killed bacilli is therefore apparent. It is believed by some that the use of the living sensitized bacilli for vaccination might produce carriers, therefore sensitized killed bacteria are practically used exclusively in the preparation of the sensitized vaccine on the market.

The claims made by Besredka and his followers in behalf of sensitized bacterial vaccines are as follows:

1. As a rule they produce but slight local reaction (inflammation at the site of injection). This rule has its exceptions. Occasionally severe local reactions follow their injection. However, this is not as likely to occur when using the sensitized bacterin as when the nonsensitized are employed.

2. They cause no general reaction. This is the rule, but it has exceptions. General reactions are manifested by malaise, increased temperature, etc.

3. They may be given more frequently and in much larger doses than the unsensitized bacterins (every twenty-four to forty-eight hours). Occasionally persons are found who cannot digest larger doses. In such cases the dose should be decreased.

4. The immunizing effect is almost immediate, manifesting itself within from 24 to 48 hours), instead of 9 to 10 days.

5. The course of treatment for immunizing an individual against typhoid fever used by the U. S. Army is to inject 500,000,000 killed typhoid bacilli subcutaneously, to be followed 10 days later by the injec-

*Ann. de l'Inst. Pasteur, 1913, xxvii, 597.

tion of the second dose (1,000 million killed bacteria), and after another interval of 10 days by the injection of the third dose (1,000 million killed bacteria). The dosage of sensitized typho-bacterin is twice as large, i.e., 1st dose 1,000 million, 2nd dose 2,000 million, 3d dose 2,000 million. Intervals 6 to 7 days. In the event of a threatened epidemic the advantages in favor of a quick acting bacterin immunity against typhoid fever are not difficult to realize.

6. According to Besredka, sensitized bacteria give results in very late stages of the disease, when no response is secured from the ordinary bacterins, and even serum treatment is ineffective.*

7. Owing to the fact that the specific bacteriolytic amboceptor is already united to the antigen (bacteria), and therefore ready for prompt digestion by the body cells when injected it follows that the body cells are saved from the effort of producing amboceptor, an effort which the body cells of a patient sick with typhoid fever may be unable to accomplish.

8. There is not the same liability of producing what is called a "negative phase"—the temporary condition sometimes following the injection of an ordinary bacterin owing to the using up of the opsonin in the patient's blood, the same being required to prepare the injected bacterin for phagocytosis.

NON-SPECIFIC PROTEINS IN THE TREATMENT OF INFECTIOUS DISEASE

Recent work of Jobling, Petersen and others tends to show that so-called foreign proteins—bacterial proteins, milk proteins and other animal proteins, vegetable proteins, etc., when used as therapeutic agents in the treatment of certain infectious diseases may prove of curative value. These non-specific proteins are slowly injected intravenously. Immediately following the injection a severe reaction usually followed by a high fever generally results, and after this severe reaction marked improvement and even permanent cure may be the outcome. It is believed by some that the high fever and increase in the ferments and leucocytes of the blood following these injections account for their good results, but it should be remembered that non-specific therapy is not bacterial therapy.

The specific value of bacterial vaccines is of paramount importance. Non-specific proteins have no immunizing value whatever. Those who advocate non-specific protein therapy admit that there is no difference between the specific and non-specific proteins provided they are given in equal doses intravenously. Why then substitute non-specific for the specific products ? They also warn the profession that the reactions fol-

*Bulletin de l'Institut Pasteur viii, 6, pp. 241-253, Mars, 1910.

lowing the intravenous use of non-specific proteins may prove a source of danger unless special precautions are observed.

The science of immunology is developing so rapidly that a more extended review even of the most recent discoveries in this field would fill a book, hence my paper, limited as it is by the rules of the Society as to time allowed for reading it and space permitted in the Transactions, is necessarily very incomplete.

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